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AN ATTEMPT TO IMMUNIZE CALVES AGAINST TUBERCULOSIS BY FEEDING THE MILK OF VACCINATED COWS.

By W. L. Moss, M. D.,

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The question of the transmission of immunity from parent to offspring—paternal transmission, maternal transmission, placental transmission and transmission through milk—has long occupied investigators and there is an extensive literature on the subject. Experiments have been made on human beings, horses, cows, goats, dogs, cats, rabbits, guinea-pigs, mice and fowls. In the greater number of the experiments antitoxic immunity has been investigated, as more exact quantitative experiments are possible with this form of immunity, but the work has not been confined to any one line and there have been many experiments reported on the transmission of agglutinins, lysins, precipitins, and other immune bodies. While there are some discordant results in the literature, it may be accepted as proven that an efficient immunity may be established against a number of infectious and toxic agents; that in the case of most of these immune bodies can be demonstrated in the blood; that these immune bodies may also appear in the milk; that from the milk they may be absorbed from the alimentary canal of the nursling and appear in the blood of the latter, where they exert a definite protective influence.

I shall make no attempt to give a complete review of the literature, but quote only a few authors in support of the above statement. Ehrlich[1] showed that immunity against abrin in mice could be transmitted through the milk to the young. He concluded that the immunity thus transmitted was passive; that it increased with the time of nursing and lasted two or three months. Ehrlich and Huebner[2] were able to show the transmission of immunity against tetanus in pigs and mice from mothers to nurslings.

Widal and Sicard[3] found that typhoid agglutinin, as well as the antitoxins of ricin, abrin and tetanus, may be transferred in mice through the milk of immune mothers to their young. Similar experiments with cats and guinea-pigs gave negative results.

Felice La Torre[4] made observations on 17 mothers who nursed 17 children. The ages of the children ranged from 1 to 24 months. The mothers all received diphtheria antitoxin after the birth of the children, 5 receiving three subcutaneous injections of 3000 units, a total of 9000 units each, and the remainder, three injections of 6000 units, a total of 18,000

units each. The blood-serum of the children was examined before the mothers received antitoxin and again three days after the last injection. In every case, regardless of age, a transference of the specific antibodies to the blood of the children could be demonstrated, but in such small quantities that the author did not consider this method of value either for prophylactic or curative purposes.

Römer and Much [5] showed that tetanus antitoxin, injected subcutaneously into cows, was capable of being transmitted through the milk to young calves and could be demonstrated in the blood of the latter.

Much [6] demonstrated the transmission of tetanus antitoxin through the milk from human mothers to their infants.

Hamburger [7] injected tetanus antitoxin into a rabbit three hours after she had given birth to young and was able to demonstrate antitoxin in the rabbit's milk and subsequently in the blood of the young rabbits fed on this milk.

Hamburger [8] repeated some of Ehrlich's experiments and was able to confer a high grade of immunity to young mice against ricin by causing them to nurse immune foster-mothers.

Römer [9] demonstrated the transmission through the milk of tetanus antitoxin from a mare to her colt. The mare was immunized 25 days after the birth of the colt.

That an active immunity against tuberculosis may be established in cattle has been proven by Pearson and Gilliland,[10] von Behring, Theobald Smith [11] and others.

As early as 1903 von Behring [12], [13] suggested the possibility of conferring upon infants a passive immunity against tuberculosis by feeding them on the milk of vaccinated cows.

I have not been able to find in the literature the report of any experiments which seem adequate to decide this question. In a personal communication dated February 3, 1908, from Dr. Leonard Pearson to Dr. J. H. Knox, Jr., which was kindly placed in my hands by Dr. Knox, I find the following statements:

> **Von Behring has claimed that the milk of cows immunized to tuberculosis carries immune bodies which are absorbed without change by those fed upon such milk, with the result that resistance to tuberculosis is increased. I do not know of any experiments on a sufficiently large scale to throw important light on this subject. So far as I am aware, von Behring has not published the experiments upon which his conclusion is based.**
>
> **We have made at the laboratory of the State Livestock Sanitary Board a few experiments, which consisted in feeding a set of swine on the milk of immunized cows and another set of swine on the milk of untreated cows. Subsequently both sets of swine were exposed equally to tuberculosis by feeding cultures. The exposure, as measured by its effects, was rather slight, but still there was a difference in the two sets of swine as shown by post-mortem examination. In one lot there were lesions of tuberculosis in the mesenteric lymphatic glands, while no lesions were found in the swine that had received the milk of immune cows. We have intended for some time to repeat this experiment, but have not yet been able to do so.**

In view of the importance of the question the experiments which form the basis of this report were undertaken.

Object.—To determine if calves can be immunized against tuberculosis by feeding the milk of vaccinated cows.

Method to be Employed.—Six calves of approximately the same age, weight and breed to be selected from healthy, non-vaccinated cows. Three of these calves to be fed from birth with the fresh mixed milk of several vaccinated cows. The three remaining calves to be fed during the same period with an equal amount of fresh mixed milk from non-vaccinated cows, proven by the tuberculin test to be free from tuberculosis. At the end of several months all six calves to be inoculated with a medium dose, lethal for normal calves, of bovine tubercle bacilli. The feeding of all calves to be continued as previously until the termination of the experiment. At the conclusion of the experiment all calves to be autopsied and the lesions present compared.

The general plan of procedure outlined above was followed in two separate series of experiments. The second series was undertaken after the completion of the first and with certain modifications that will be indicated.

Selection of Calves.—The calves used in any one series of experiments were of the same breed, within a few days of the same age and, at the beginning of the experiment, were of approximately the same weight. It was, of course, necessary to exclude, as far as possible, the use of calves already infected with tuberculosis. To accomplish this the calves were obtained from a herd in which no tuberculosis was known to exist and their dams were tuberculin-tested shortly after the calves were dropped. In no case was a positive reaction obtained.

The Vaccinated Cows.—The vaccinated cows furnishing milk for the first series of calves were immunized as heifers about 18 months before the feeding experiments were started. Their treatment consisted in four intravenous injections of a suspension of living tubercle bacilli of the human type. The suspension used was made in a salt solution, was freed from clumps by centrifugalization and was approximately of the density of a 24-hour broth culture of B. typhosus. The first dose consisted of 1 cc. of this suspension; the second dose of 2.5 cc.; the third dose of 4 cc. and the fourth dose of 6 cc. The interval between doses was about three weeks. For the second series of experiments an attempt was made to hyperimmunize the vaccinated cows; a series of ten vaccinations was given, beginning March 7, 1909, and ending May 12, 1910. Injections were made intravenously and consisted of a suspension of tubercle bacilli of human type, prepared as in the preceding series. The dose was gradually increased from 1 cc. at the first injection to 5 cc. at the last injection. The feeding experiments with the milk of these cows were begun ten months after the vaccinations were completed.

Examination of Milk of Vaccinated Cows for the Presence of Tubercle Bacilli.—An examination was made to determine if any of the vaccinated cows were shedding tubercle bacilli in their milk at the time these experiments were started. Microscopic examination of the sediment obtained after prolonged centrifugalization at high speed and guinea-pig inoculations of both cream and sediment from the milk failed to reveal the presence of tubercle bacilli.

Non-Vaccinated Cows.—The non-vaccinated cows furnish-

ing milk for these experiments were healthy animals, shown to be free from tuberculosis by the tuberculin test.

Feeding and Care of Calves.—The calves were nourished by their mothers during the first few days of life until the number requisite to complete the series could be obtained. A new pasture was enclosed by a double fence, a space of about 15 feet being left between the two fences. A double fence divided the pasture into two equal parts, separated by about 15 feet. A new barn was erected on each half of the pasture for the protection of the calves. The group of calves which was to receive the milk from the vaccinated cows was placed in one of these pastures and the group which was to receive the milk of non-vaccinated cows was placed in the other pasture. The two groups of calves were thus kept separated from each other and from contact with any other animals on the farm throughout the experiment. Both sets of calves were fed exclusively on milk during the first few weeks, but later it was necessary to supplement the milk feeding with hay and grain.

Test Inoculation of the Calves.—A virulent strain of bovine tubercle bacilli was used for the test inoculation. A suspension of this was prepared by thorough grinding in salt solution. The larger clumps were removed by centrifugalization and the resulting suspension was shown by microscopic examination not to contain aggregates of more than three or four bacilli. This was then diluted with salt solution until it was approximately of the density of a 24-hour broth culture of B. typhosus.

The first series of calves received 1 cc. of such a suspension into the anterior jugular vein as a test inoculation. The second series was tested with a subcutaneous injection of 1 cc. of such a suspension behind the right scapula.

First Series of Experiments.

(This series was started on May 21, 1909.) Six calves were obtained at birth from healthy cows, proven to be free from tuberculosis by the tuberculin test, which was given after the cows had dropped their calves. The calves were divided into two groups of three each, as nearly equal as possible as regards weight and general condition. They were placed in separate pastures and kept thus separated throughout the experiment. To one group was fed the mixed milk of several immunized cows. To the other group was fed the milk of non-immunized healthy cows. The feeding was continued until October 4, 1909, at which time all six calves received intravenously 1 cc. of a suspension of virulent bovine tubercle bacilli. The feeding was continued as previously until the conclusion of the experiment. Following the test inoculation the calves rapidly developed the infection, with loss of weight, roughening of the coats and cough. All six calves died in the fourth week after inoculation. At autopsy the lesions were practically identical in every case. It is therefore unnecessary to give in detail the autopsy findings. Briefly, all showed massive tuberculous pneumonia. The only other macroscopic lesion consisted of an eruption of sub-endothelial tubercles in the right side of the heart. Microscopically miliary tubercles were found throughout the other organs of the body, the spleen, liver, kidneys and lymph glands. It is evident from this result that the infecting dose was excessive and masked any difference in immunity which may have been present in the two sets of calves. The autopsy findings in these cases are of interest in indicating the fate of the injected bacilli. Although the suspension was practically free from clumps, and any which it may have contained were probably much smaller than a red blood cell, it seems likely that all of the bacilli were arrested in the lungs except those which found lodgment in the right side of the heart and produced the sub-endothelial tubercles present in this situation. The microscopic findings, in the tubercles present in the other organs, indicated that they were formed at a later date and probably resulted from the discharge of bacilli into the systemic circulation, due to the erosion of the pulmonary veins by the lesions in the lungs. A probable explanation for the failure of the injected bacilli to pass through the pulmonary circulation is that they were agglutinated on being introduced into the blood stream. In this connection some experiments from the Bureau of Animal Industry are of interest. A fine suspension of lamp black, the individual particles of which were much smaller than red blood cells, was prepared and injected intravenously into rabbits and a horse. Death followed the injection of comparatively small quantities of this suspension and autopsy showed that all the lamp black had been filtered out in the lungs. It seems not improbable that this result was also due to the agglutinating action of the blood on the particles of lamp black.

Examinations were made to determine if the blood of the vaccinated cows used in this experiment contained any excess of antibodies over the blood of the non-vaccinated cows from which the control calves were fed. Tests were made for agglutinins, precipitins and complement-binding bodies. Agglutinins were present in the serum of some of the members of both groups of cows, but were not present to any greater degree in the vaccinated animals. Precipitins and complement-binding bodies could not be demonstrated in the blood of any of the cows, although various antigens were employed, bacillary suspensions, extracts and tuberculins. In a similar way the blood of the two sets of calves was tested before inoculation and no difference could be determined between the agglutinating, precipitating and complement-binding action of the two groups.

On account of the failure of the first experiment, a second series was undertaken with slight modification.

Second Series of Experiments.

Six calves were obtained from healthy cows, shown to be free from tuberculosis by the tuberculin test, applied within a few days after the calves were born. These calves were divided into two equal groups. New, separate pastures and barns were prepared for them as in the preceding series and they were kept separated throughout the experiment. Feeding was begun on March 9, 1911. One group received milk from the hyperimmunized, the other group from non-vaccinated, healthy cows. On December 1, 1911, all six calves received the same dose of virulent bovine tubercle bacilli, 1 cc.

of the suspension subcutaneously, behind the right scapula. The feeding was continued as previously until the experiment was terminated. The calves receiving milk from immunized cows throve better than the other group and at the time of autopsy weighed about 25 per cent more than the controls. It is unfortunate that the three calves receiving milk from immunized cows were all bulls while the other three calves were heifers. This fact may account in part for the difference in the general condition at the conclusion of the experiment. A month or six weeks after inoculation it became evident that local lesions had been produced in all three of the calves receiving milk from the non-vaccinated cows. In one of these the lesion broke down and left a discharging sore. Subsequently these three calves showed clinical evidence of infection which consisted in roughening of the coats and retarded development. The three calves which received milk from vaccinated cows likewise developed local lesions, but careful palpation was necessary in order to reveal them.

One calf from each group was killed and autopsied on March 16, 1912. The autopsy showed as follows: The calf which had received milk from immunized cows showed a small lesion at the site of inoculation, about 2 cm. in diameter, containing caseous material and surrounded by a thick fibrous wall. The related axillary lymph glands showed small caseous nodules and there were a few caseous areas in the bronchial lymph glands. The control animal showed at the site of inoculation a caseous abscess, 6 to 8 cm. in diameter, with a thin wall. The related axillary lymph glands were enlarged and caseous, as were also the bronchial lymph glands and those in the region of the gall-bladder. The liver contained 15 to 20 caseous areas 1 to 5 cm. in diameter.

The microscopic examination of tissues from the calf which had received milk from immunized cows showed the tonsil, lung, heart, spleen, kidney (2 sections), adrenal and testis to be normal. The abscess wall at the site of inoculation showed a dense fibrous wall, 1 mm. thick, lined with a layer of very vascular tubercular granulation tissue. A section of one lymph gland showed two healed tubercular lesions, 2 mm. in diameter, and about the periphery smaller tubercles of more recent origin. The calf receiving milk from non-immunized cows showed at the site of inoculation a fibrous wall about the same thickness as the above, the granulation tissue lining it being less vascular and containing fewer giant cells than in the preceding case. The tissue surrounding the abscess, consisting of connective tissue, fat and voluntary muscle, showed a very acute inflammatory process containing fibrin and polymorphonuclear leucocytes with recent tubercles scattered throughout. Evidently a mixed infection had been present. Two lymph glands were examined; one showed a small tubercle; the sinuses of the other showed numerous giant cells without any definite tubercle formation. The liver showed numerous conglomerate tubercles of both the proliferative and exudative type. The spleen showed well-marked conglomerate tubercles of the proliferative type. Sections from the lung, heart, kidney and ovary were negative.

A second pair of calves was killed and autopsied on December 13, 1912. The one that had received milk from vaccinated cows showed at the site of inoculation a tuberculous lesion, 3 to 4 cm. in diameter, with a thick fibrous wall. The retropharyngeal lymph glands were about 3 cm. in diameter and contained a few small tubercles. The liver contained four nodules, 1 to 3 cm. in diameter. The control animal showed at the site of inoculation a tuberculous abscess, 10 to 12 cm. in diameter, which had infiltrated the surrounding tissue. The axillary and prescapular lymph glands on both sides were tuberculous, as were also the retropharyngeal and bronchial lymph glands. Scattered throughout both lungs were areas of tuberculosis which measured up to 1 cm. in diameter. The liver contained a number of caseous areas from 1 to 5 cm. in diameter.

The microscopic examination of tissues from the calf which had received milk from immunized cows showed the lung, heart, kidney, a hemolymph node and a section from one of the serous glands free from tuberculosis. The report on sections from the lymph glands examined was in seven instances negative for tuberculosis; in two instances "no definite tuberculosis"; and in one case "a few healed tubercles (?)." The liver showed numerous miliary and conglomerate tubercles; in places extensive caseation and calcification. The spleen showed small scattered areas containing small round hyalin masses and epithelial cells (venous thrombi); no caseation, no giant cells. The abscess wall at the site of inoculation showed scar tissue, containing some caseous and calcified areas. Microscopic examination of tissues from the control calf for the preceding, which had been fed the milk of non-immunized cows, showed at the site of inoculation a very thin layer of scar tissue enclosing tuberculous granulation tissue and caseous material. A section consisting of connective tissue, fat and voluntary muscle from outside the abscess wall showed a large mass of tuberculous tissue with areas of caseation and calcification. Sections from four lymph glands examined showed extensive tuberculosis. Section from the lung showed an encapsulated tubercular mass with a few small proliferative tubercles scattered elsewhere. The liver showed tuberculosis and the spleen showed small recent miliary tubercles. Other organs examined were negative for tuberculosis.

The two remaining calves were killed and autopsied on December 16, 1912. The one which had fed upon milk from the vaccinated cows showed at the site of inoculation a tuberculous abscess, approximately 3 by 6 cm., surrounded by a thick fibrous wall. No other macroscopic lesions were discovered except four nodules in the liver, which varied from 1 to 3 cm. in diameter. The control animal showed minute caseous areas in the retropharyngeal and bronchial lymph glands, and scattered throughout both lungs were numerous areas of tuberculosis measuring up to 1 cm. in diameter.

Microscopic examination of the tissues from the calf which had received milk from immunized cows showed the lung, heart, liver and testis free from tuberculosis. Of the sections from 12 lymph glands examined, 9 were free from tuberculosis. Two showed a few small, indefinite tubercles and one showed extensive tuberculosis. The report on the spleen was, "Small

recent, indefinite tubercles (?)." The abscess wall consisted of fibrous and tubercular tissue containing caseous and calcareous material. Microscopic examination of the tissues from the control calf for the preceding, which had received milk from non-immunized cows, showed tuberculosis in a section removed from the site of inoculation, containing striated muscle and lymphoid tissue. Of 13 lymph glands examined microscopically, 4 showed tuberculosis. The liver contained numerous conglomerate tubercles. The spleen contained small scattered tubercles. A section from the heart and two sections from the lungs showed no tuberculosis.

As in the preceding series, the blood of the two sets of cows furnishing the milk for these experiments was tested for tuberculo-antibodies. No difference could be determined by means of the agglutinin, precipitin and complement-binding tests. Nor did similar tests show any difference between the blood of the two sets of calves.

The result of the second series seems to justify the conclusion that a relative degree of immunity against tuberculosis may be conferred upon calves by feeding the milk of vaccinated cows. Further experiments are necessary to determine if human beings may be similarly influenced.

The experiments reported above were suggested to me by Mr. S. M. Shoemaker, of Eccleston, Md. It is a pleasure to acknowledge my indebtedness to Mr. Shoemaker, not only for his generosity in defraying all the expenses of the work, but also for many valuable suggestions in the actual conduct of the experiments.

I am also indebted to Dr. S. H. Gilliland, of Marietta, Pa., who performed all of the vaccinations on the cows used in these experiments, as well as all of the tuberculin tests. He also prepared the suspensions of virulent bovine tubercle bacilli and gave the test inoculations to the calves.

For the microscopic examination of the tissues removed at autopsy, I am indebted to Dr. Thos. P. Sprunt, of Baltimore.

I am further indebted to Dr. Wm. H. Welch, of Baltimore; Dr. Theobald Smith, of Boston; Dr. E. R. Baldwin, of Saranac Lake; and Dr. S. H. Gilliland, for their interest and helpful suggestions in the work.

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COMPLEMENT FIXATION IN THYROID DISEASES.[1]

By SYDNEY R. MILLER, M. D., and RUTH E. FAIRBANK.

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Perhaps no field of research has been more vigorously worked in recent years than that which deals with the subject of *functional diagnosis*. With an ever-increasing knowledge of the physiology of the various glandular organs of the body and a wider recognition of the part which they play in various diseases, attempts have been made to devise clinical tests which would give accurate information as to the extent to which any given gland was performing its normal duties. Numerous examples might be mentioned, such as the desmoid test of Sahli, Strauss' levulose tolerance test for hepatic insufficiency, Schmidt's nuclei test for pancreatic activity, and finally the well-known phenol-sulphon-phthalein test of Rowntree and Geraghty which, as applied to the diagnosis of renal conditions, probably represents to-day the best and most highly specific of all laboratory functional diagnostic methods. It is not at all surprising, in view of the growing interest in the endocrine glands, that attempts have been made to discover methods for the recognition of normal and abnormal activity in them. The problem here, however, is obviously a much more complex one than that which deals with glands possessing ducts, for the endocrine glands are so intimately connected one with the other, either through the agency of the central nervous system or through the action of their specific hormones, that it is extremely difficult, while attempting to study the function of any one particular gland of internal secretion, to eliminate the influence of all the others.

Probably by reason of the frequency with which disorders of the thyroid gland occur, the most vigorous studies have

[1] Reported before The Johns Hopkins Hospital Medical Society, Dec. 7, 1914.

been put forth toward understanding the functioning of this gland in health and disease, and particularly because, although the clinical manifestations of dysthyreosis are in so many instances easy to recognize, in another large group the evidence is often tangibly inconclusive, despite the fact that suspicion may amount almost to certainty in the mind of the observer. All the other endocrine glands as well have been studied with great care and methods devised which, though still imperfect, are very helpful in arriving at a diagnosis when taken in conjunction with careful clinical and experimental studies. Writing in the early part of 1914, Dr. Barker[1] called attention to the fact that there existed at that time four so-called functional tests for thyroid activity which, though usually positive in outspoken cases of Graves' disease, are almost always negative in the milder types, the so-called *formes frustes*. Brief reference to these four tests may be of interest.

1. *The Acetonitrile Test* of Reid Hunt[2] first described in 1905. In a series of well-controlled experiments Hunt was able to demonstrate that white mice fed on thyroid extract in the form of Ehrlich cakes became much more resistant to the toxic effects of hypodermic injections of acetonitrile, a drug which is poisonous by reason of its slow liberation within the body of hydrocyanic acid. If the animals were first fed on the blood of thyroidectomized animals, they failed to show this increased drug resistance. In a large series Hunt noted no such resistance to other drugs which were tried, morphine excepted. Trendelenburg[3], in 1910, was able to confirm Hunt's findings, and further amplified them by showing that white mice fed on blood taken from patients suffering from Graves' disease also became more resistant to the injection of the drug. Ghedini,[4] in reviewing the work in 1911, was not only able to demonstrate the truth of Hunt's observations, but also noticed that a similar increased resistance followed the feeding of blood-serum taken from patients suffering from chronic nephritis and a number of other conditions which were not in any way apparently associated with thyroid hyperactivity.

2. *The Demonstration of Hyperadrenalinemia.*—Though numerous chemical methods had been introduced to detect quantitatively the presence of adrenalin in the circulating blood, it remained for Fraenkel[5] to demonstrate, in 1909, an increase in this substance in the blood of patients suffering from exophthalmic goiter. His test consisted in comparative observations upon the strength and frequency of contractions of isolated rings of the excised uterus of rabbits when immersed in oxygenated Ringer's solution, human serum and adrenalin solutions. Since then a number of other methods, all of a biological type, have been employed to demonstrate an increase of adrenalin in the blood. Of these the following may be mentioned:

(a) The test of Melzer and Ehrmann,[6] which is based upon the production of mydriasis when adrenalin is instilled into the enucleated eye of a frog.

(b) Cameron,[7] as the result of her investigations, concludes that the best method for testing the blood concentration of adrenalin is by determining the effect upon the blood pressure of rabbits which have been previously atropinized.

(c) Hoskins[8] has devised a method based upon the fact that adrenalin inhibits the movements of the isolated loop of a rabbit's intestines in oxygenated Ringer's solution.

(d) Based upon the fact that adrenalin constricts a strip of peripheral artery and causes relaxation in a strip of the coronary artery, Janeway and Park[9] have devised a method by means of which one part of adrenalin in 50,000,000 parts of Locke's solution or in 20,000,000 parts of blood may be detected.

All these biological methods doubtless demonstrate the presence of an increased adrenalin content, nevertheless they are hypersensitive, not particularly easy to carry out as routine clinical tests and, moreover, they vary tremendously when applied to various normal individuals. Falta[10] even doubts whether these reactions are specific for adrenalin at all. Though it has been shown that the intravenous injection of thyroid substance does produce an increased adrenalinemia, it has not been shown that an increased adrenalin content is a constant feature of Graves' disease, while, on the other hand, such an increase has been found in a number of other states, notably states of emotion, especially of fear, a point brought out more particularly by the researches of Cannon.[11] With reference to these first two functional tests mentioned, Eppinger[12] states that, although they are of considerable scientific interest, they as yet possess no definite clinical value.

3. *Abderhalden's Dialysis Test.*—Since the publication, in 1912, of Abderhalden's[13] dialysis method for the demonstration of protective ferments in the blood, the test with its underlying principles has been applied to almost every conceivable condition. The results thus far have been discordant in the hands of many observers, and the exact clinical and scientific status of the test still remains an undetermined factor. Lampé and Fuchs[14] have used the test quite extensively in the study of Graves' disease and other thyroid conditions. From their studies of some sixty cases, they arrived at the following conclusions:

(a) The serum from a case of Graves' disease splits a substratum of Basedow thyroid tissue consistently, and occasionally may split normal thyroid tissue as well.

(b) The same serum is generally capable of splitting substrata prepared from the thymus and sex glands.

(c) Practically the same results are observed in "Basedowoid cases" or cases of simple hyperthyroidism.

(d) Sera from cases of myxœdema and endemic goiter are also capable of splitting thyroid tissue.

From these findings they came to the opinion that in Graves' disease there is both a hyper- as well as a dys-functioning of the thyroid and of the sex glands as well, and that in myxœdema and endemic goiter also, there is present a dysthyreosis, but one of a different type, the nature of which is still obscure. Up to the present time their work has not been confirmed, and the clinical value of the entire Abderhalden technique, more particularly as regards its specificity as an indication of the dys-functioning of the thyroid or of any other organ, is as yet undecided.

4. *Roseo's*[15] *Complement Fixation Test.*—The application of Roseo's name to this particular test is apparently unwar-

ranted, for in an article by Papazolu,[10] written in 1911 on the same topic, reference is made to complement fixation tests performed in 1908 by Marinesco. Apparently his work was not published, but was continued by his pupil, Papazolu, who in 1911, by using etherial extracts of thyroid tissue removed at operation, obtained complement fixation with the sera of 26 out of 38 cases of Graves' disease; the same sera gave no fixation with antigens prepared from normal thyroid or parenchymatous goiter. In another monograph referred to by Klose,[11] the same author reports positive reactions in 58 out of 60 cases of Graves' disease. He further noted that some luetic sera, used as controls, bound complement in the presence of the etherial extract of normal thyroid tissue; and he came to the conclusion that in exophthalmic goiter the dysfunctioning gland acts as an antigen and causes the production of antibodies demonstrable by the Bordet-Gengu phenomenon. In 1913 Roseo reported the results secured by using the aqueous extracts of two Basedowian thyroids, the work being a continuation of some earlier observations of his upon this same reaction. He reports positive results with both antigens in four out of five cases of classical Graves' disease. Of these cases, however, two gave a positive Wassermann reaction, though five known luetic sera were negative as tested with both thyroid antigens. No details of the methods of control for these tests are given. Both Papazolu and Roseo agree in stating that the reaction is negative in the abortive forms.

Numerous other studies have been made upon the bio-chemistry of Basedowian blood. Kottman [12] and Lidsky and others have found that the coagulation time is increased, and that this change can be induced by injections of potassium iodide or of thyroid substances, an observation confirmed in Klose's clinic. The reverse condition has been observed in myxœdema, and hence this test is considered of some differential diagnostic value. Since the thyroid secretion increases the metabolism of the body, the blood contains an excess of protein-split products and hence the freezing point of the blood is lowered, a fact also observed by Klose. Hyperglycemia has been observed quite constantly in Graves' disease and by many is explained by the increased adrenalin content. Wälli [13] has found a constant increase in the anti-trypsin content of the blood in cases of Graves' disease, this increase being manifested even in the earliest stages and long before the cardinal symptoms are prominent. The index varies directly with the stage of the disease.

Of the four functional tests referred to by Dr. Barker, the last one seemed the most likely to yield conclusive results and the present report deals with a study of its value.

METHODS AND MATERIALS EMPLOYED.

(A) *Antigens.*—All of the antigens used were prepared from thyroid tissue which was secured at the time of operation from patients suffering with outspoken Graves' disease. That such was the case was always confirmed by a careful analysis of the patient's clinical history, subjective and objective findings, and parallel observations upon the histology of the tissues in question. The thyroid tissues were secured through the kindness of Dr. Halsted and Dr. Finney of this clinic, and through the hearty cooperation of Dr. E. F. Butler of the Mayo Clinic, and of W. J. Rogers of Dr. Crile's service at Lakeside Hospital, Cleveland. To all of these we express our thanks for the specimens and records furnished us.

As soon after removal as possible the tissues were weighed and, where possible, were divided into two or more portions, so that from one and the same gland two or three different types of antigen could be prepared. The specimens received from Cleveland and Rochester were in sealed, sterilized containers, and showed no evidence of autolysis at the time that they were received. In general the tissue extracts or antigens were made up in proportions similar to the original formula used by Wassermann in the reaction which bears his name. In other instances the tissues were extracted with 2, 5 or 10 volumes of the fluids used. The various types of antigens thus prepared were of the following nature:

(a) Aqueous: Made up with sterile, normal saline and preserved by the addition of suitable small amounts of tricresol.

(b) Alcoholic: 95 per cent and absolute alcohol were both employed.

(c) Acetone.

(d) Extracts obtained with equal parts of alcohol and ether.

(e) Aqueous and alcoholic extracts sensitized by the addition of Bayer's iodothyrin.

(f) Alcoholic extracts strengthened by the addition of .1 per cent iodin.

In most instances the antigens were prepared by a preliminary shaking process followed by incubation for from one week to ten days at 37° C. Prior to the use of any antigen it was carefully tested in the usual manner for the following points: (1) Whether it was capable of producing hemolysis alone; (2) whether it was anticomplementary, and if so, in what dilution; and (3) whether it was capable of fixing complement in the presence of a normal serum.

(B) *Sera.*—The sera to be tested were all secured either by the usual method of venous puncture or were obtained at the time of operation directly from one of the thyroid arteries. After centrifugalization, the sera were inactivated at 56° C. for half an hour and diluted 1-5 with normal salt solution, after which they were tested in the following ways:

(a) Wassermann examinations were made, each serum being tested against three different antigens of the following nature, namely, an alcoholic extract of luetic liver; an alcoholic extract of human heart; and, finally, a similar extract sensitized with .4 per cent cholesterin.

(b) Every serum was tested against each of the thyroid antigens, 19 in all, each antigen being in five different dilutions, namely, 1-5, 1-10, 1-20, 1-30, and 1-40. In cases where spinal fluids were employed, no inactivation nor dilution of the fluid was resorted to. Throughout the work complete hemolysis was represented by a cipher, complete fixation or inhibition of hemolysis by the figure 4; the unit of volume chosen was .2 cc. Complement was secured from the guinea-pig, and an anti-sheep amboceptor of high hemolytic titre was employed. Suitable amboceptor and complement titra-

tions were run preliminary to each series of thyroid-fixation tests.

RESULTS.

The cases which have been submitted to tests against the thyroid antigens above described fall into six definite groups:

(a) Cases of true Graves' disease. The blood for these cases was always secured prior to operation. This group includes cases also of acute exophthalmic goiter, a typical history of one of which is as follows:

K. H., male, aged 38, was admitted, complaining of nervousness. He presented a remarkable family history in that his mother had had simple goiter for many years, his eldest sister had been operated upon for Graves' disease, and his eldest daughter was suffering from the same malady. In good health up until one month previously, he suddenly became nervous, noticed an increase in the size of his neck, was very irritable, had palpitation of the heart, shortness of breath, and his friends noted a bulging of his eyes. His appetite had increased markedly, though his weight had fallen off perceptibly. All of these symptoms had increased up until the time of admission. When he entered the hospital his pulse was 146, his respirations were 22, and the objective findings of exophthalmic goiter were marked in every respect.

(b) Cases not outspokenly exophthalmic in type, but diagnosed clinically as instances of hyperthyroidism.

(c) Cases showing unexplained tachycardia. These were all observed in the Phipps Psychiatric Clinic and in no instance was there any demonstrable involvement of the cardiac muscle. The cases in question fall into scattered clinical groups.

(d) In view of the findings of numerous investigators who have applied the Abderhalden technique to the study of cases of dementia præcox, it seemed worth while to attempt the application of complement fixation methods to a series of such cases.

(e) Sera from a group of patients known to be syphilitic. All of these sera gave complete fixation with the Wassermann reaction and were secured from patients in all stages of the disease.

(f) Spinal fluids employed in the present study were all taken from undoubted cases of general paresis.

The results of the complement fixation reaction in the present study are clearly shown in Table I. An examination of this table shows that the results have been *consistently negative in all except the luetic cases.* In other words, there has been no evidence of complement fixation except in the case of those sera or spinal fluids which were known to have had and were proved to have a positive 100 per cent Wassermann reaction. This fact affords further evidence of interest with reference to the non-specificity of the Wassermann reaction and raises some new questions as to the nature of the reacting substances in this valuable test. Only one opportunity was afforded to note how luetic sera would react with an antigen prepared from a normal thyroid, but the evidence, as based upon the testing of some ten or twelve positive sera against it, was all on the negative side; that is, no fixation was secured. The weight of evidence at present is in favor of the view that the Wassermann reaction is essentially one in which the lipoid bodies are particularly concerned. As yet no observations upon the lipoid content of the Basedowian thyroid have been found in a search through the literature. It is of interest in passing to call attention to the fact that unsaturated fatty acids are important in the Wassermann reaction, for it is known that the antigen value of the acetone insoluble fraction of the tissue lipoids varies, according to Noguchi and Bronfenbrenner,[20] almost directly with its power to combine with iodin.

The idea that complement-fixation methods might be of value in thyroid and other glandular conditions is to be found in certain works published by Stephan and Oeller [21] upon the

TABLE I.

SHOWING THE NUMBER OF COMPLETE FIXATIONS GIVEN BY EACH OF 19 DIFFERENT THYROID ANTIGENS AS TESTED AGAINST 58 CASES OF VARIOUS TYPES.

Types of Antigens.		Aqueous Antigens.							Aqueous extract plus 1% iodothyrin.	Alcoholic Antigens.					Alcoholic extract plus .1% iodin.	Alcoholic extract No. 99597 plus iodothyrin.	Alcoholic ether extract. Equal parts No. 46677.	Acetone Antigens.			Positive Wassermann in blood or spinal fluid of the cases examined.
Number of cases.	Type of cases.	93663.	99597-A.	100345.	Calep.	Smith.	46371.	99738.		47089.	99786.	99597-B.	99663-A.	99647.				99993-B.	67882.	99846.	
2	Acute Graves' disease	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	Exophthalmic goiter	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	Hyperthyroidism	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	Simple goiter	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	Unexplained tachycardia	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	Dementia præcox	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
22	Luetic sera	0	0	0	2	2	0	0	0	0	21	21	20	21	0	0	20	22	22	22	22
6	Paretic spinal fluids	0	0	0	3	3	0	0	0	0	6	6	6	6	0	0	6	6	6	6	6

value of the Abderhalden reaction. These authors were able to show that, if a serum capable of splitting a given substratum is first inactivated, it is thereby rendered inert, but that it may be made to refunction by the addition of guinea-pig's serum, in other words, complement. As a result of their experiments, they came to the conclusion that ferments in the sense that Abderhalden uses the word, do not exist as such, but are nothing more than amboceptors in the sense in which Ehrlich first introduced this term. They were inclined to believe that the method of complement fixation could be used for the demonstration of antigen-antibody reactions of many kinds, and in fact were able to apply this method successfully in the diagnosis of pregnancy. They believe that the human body is, in states of disease, autosensitized with the products of abnormal intermediate metabolism, or with the perverted secretions of one or more of the endocrine glands, and that war is constantly being waged upon the endogenous toxins thus produced. In response to each autosensitizing abnormal product or antigen, specific antibodies are produced, which are rendered inert by their fixation with the patient's own complement. Assuming that this were the case, suitable methods of the application of the Bordet phenomenon should be capable of revealing which organ or gland in the body is responsible for the symptoms which clinically are referred to it.

The results here reported are at marked variance with those of Roseo and Papazolu; Roseo's paper is singularly meager in the description of the technique employed and his results are based upon a very small series. With reference to Papazolu's positive findings, it should be noted that he employed etherial extracts as antigens; just how these were made to mix with the other components of the test is not stated—nor how evaporation was prevented during incubations. Though the series here reported is not large, the cases chosen are all of a classical type; and it is felt that the testing of each serum against so many different antigens is more than equivalent to a larger number of sera tested with but one or two extracts of the same nature.

The method as employed here with suitable controls has been singularly unproductive and we are therefore of the opinion that the complement fixation test of Roseo is of absolutely no value as a clinical measure in determining the existence of hyperthyroid states or conditions of dysthyreosis.

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TWO PHYSICIAN-ECONOMISTS.[1]

SIR WILLIAM PETTY, 1623-1687; FRANÇOIS QUESNAY, 1694-1774.

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[NOTE.—The authoritative biography of Petty is Lord Edmond Fitzmaurice's "The Life of Sir William Petty, 1623-1687, chiefly derived from private documents hitherto unpublished" (London, 1895). Professor Charles H. Hull's definitive edition of "The Economic Writings of Sir William Petty, together with the Observation upon the Bills of Mortality, more probably by Captain John Graunt" (Cambridge, 1899), contains a wealth of biographical and bibliographical detail, as well as a convincing determination of the Petty-Graunt controversy, and a complete bibliography of Petty's published writings (pp. 633-660).

Quesnay's life and work can best be approached through Georges Weulersse, "Le Mouvement Physiocratique en France" (Paris, 1910), and thereafter studied at first hand in Auguste Oncken's "Oeuvres Economiques et Philosophiques de F. Quesnay, fondateur du système physiocratique, accompagnées des éloges et d'autres travaux biographiques sur Quesnay par différents auteurs" (Francfort et Paris, 1888). Brief but excellent outlines of Quesnay are contained in Lavergne, "Les économistes français du dix-huitième siècle (Paris, 1870) and in Higgs, "The Physiocrats" (London, 1897). An annotated bibliography of Quesnay's writings is included in Oncken, pp. 809-814.

In connection with the reading of the present paper, there were shown the original editions of Petty's notable economic works from the writer's collection, and also the more important of Quesnay's medical works from the library of the Surgeon-General's Office. The mezzotint portrait of Petty by Smith after Closterman's painting, and Will's line engraving of Quesnay after Chevallier's portrait, were also exhibited.]

The interrelation of social philosophy and medical science is a commonplace of current thought. This connection is three-fold in kind: a parallelism in scope, an association in

[1] A paper read before the Historical Club of The Johns Hopkins Hospital on March 8, 1915.

content, and a contact in doctrinal history. The writings of Darwin, Spencer, and Huxley have made such terms as "social organism" and "economic evolution" familiar phrases in economic composition. There is, indeed, no radical novelty in this mode of expression. From Aristotle's description of man as a political animal, the curious will find a recurrent anticipation of "the biological analogy" in socio-economic literature.

Not only is the social body comparable in structure and in function to the human body, but the disorders of society are analogous to the diseases of man. There is thus a social pathology with its implications of social diagnosis, social prognosis and preventive social treatment. It is astonishing how early and with what clearness this parallelism was set forth. More than three hundred years ago an earnest economic writer, Gerard De Malynes, making inquiry into "the canker of the commonwealth," declared upon the title page of his tract that, "the Author imitating the rule of good Phisitions, First, declareth the disease. Secondarily, sheweth the efficient cause thereof. Lastly, a remedy for the same."[2]

More important than the analogy in scope is the intimate association in content, of economics and medicine. The standard of living, the principle of population, the dependence of industrial efficiency upon food and working hours—suggest the recourse of social philosophy to medical science. On the other hand, occupational disease, the less spectacular but more tragic ravages traceable to insufficient wage income, the possibilities of public expenditure in the prevention of disease—point to the necessary reliance of the physician upon economic philosophy. Indeed, the neglect of this kinship has, on more than one occasion, proved hurtful. The economist would have qualified his generalization as to the necessary level of a socially desirable wage by fuller acquaintance with modern dietetics in relation to the nutritive quality of food materials. The physician would have been more guarded in his advocacy of the sanitarium as the essential weapon in the social campaign against tuberculosis had he made more intimate study of the amount and regularity of the workingman's income.

Tempting, however, as are such matters of parallelism and interrelation, it is exclusively with the third of the connections noted between economics and medicine—the contacts in doctrinal history—that I propose briefly to engage your attention. By "contacts," I mean not the mutual indebtedness of economic doctrines and medical theories, a phenomenon already referred to as "association in content," but rather the circumstance that there have been, from time to time, individuals who have attained distinction both as political economists and as physicians, and whose contributions in each field—bearing in mind the essential unity of intellectual effort—may be conceived as influencing the contributions in the other.

It would be an inviting task to attempt a reasonably complete catalogue of such physician-economists. We should think of John Locke, philosopher and statesman—the friend of Sydenham and the physician of Shaftesbury—whose contributions to medical practice were generously appraised by Sir William Osler at the celebration of the bicentenary anniversary of Locke's death held at this University ten years ago;[3] but whose notable services to economic science in establishing the foundations of modern monetary theory in the famous recoinage discussion of 1690-96 and in laying the basis of modern theories of private property and economic value, were curiously omitted.

There would be Nicholas Barbon—the son of Praisegod Barebone—student of Leyden, graduate of Utrecht, and honorary fellow of the College of Physicians. Instrumental in establishing the first fire insurance office in London, a member of Parliament, active in re-building the city after the great fire, and a projector of the short-lived national land bank that paved the way for the Bank of England in 1694, Barbon found time to write notable tracts on trade and currency whose ingenuity Bauer regards as memorable in "der Vorgeschichte der klassischen Oekonomik"—before dying in 1698, having appointed John Asgill, the economist, to be the executor of his will, and having directed that none of his debts should be paid.[4]

We should give a place to Bishop Berkeley—theologian, philosopher, idealist—author on the one hand of "The Querist," perhaps the most thoughtful economic composition of the first half of the eighteenth century, and on the other hand, of "Siris," that curious intermixture of "philosophical reflexions" and "inquiries concerning the virtues of tar water"—from which grew the war of pamphlets as to the efficacy or otherwise of this homely specific, which figures at least amusingly in the history of English medicine.[5]

[2] Gerard De Malynes, "A Treatise of the Canker of Englands Commonwealth" (London, 1601).

[3] November 1, 1904. No report of the celebration—at which Locke's contributions to philosophy, psychology, toleration, politics and social philosophy were described by distinguished scholars—appears to have been published. Sir William Osler's address on "John Locke as a physician" appeared in the *Lancet*, October 20, 1900, ii, 1115-1123, and was reprinted in "An Alabama Student, and Other Biographical Essays" (Oxford, 1908). Dr. Osler has been kind enough to write me further: "I am much interested in Petty. I picked up his MS. letter book, 1661-84, and at the back found, bound in, the agreement with Fleetwood to do the Down Survey. I gave it to Trinity College, Dublin. I have a very good collection of his original works, including the Survey. He was a remarkable man, one of the most distinguished professors Oxford ever had. It was a great loss to medicine when he got mixed up with Irish affairs."

[4] Barbon's life and economic writings are described by Dr. Stephen Bauer in Conrad's *Jahrbücher für Nationalökonomie und Statistik* (Jena), XXI. Bd. N. F., pp. 561-590; also by the same writer in "Dictionary of Political Economy" (ed. Palgrave), *sub nom.* I have reprinted (Baltimore, 1905), with an introductory word and a few notes Barbon's rare "Discourse of Trade" (1690), the title page of which bears the signature "N. B. M. D." Of Barbon's medical work, nothing is known.

[5] The history of the tar-water controversy is traced and the more important of the tracts evoked thereby is included in Professor Fraser's admirable preface to "Siris" in "The Works of George Berkeley, D. D." (Oxford, 1871), Vol. ii, pp. 343-357. "The Querist" may be found in Mr. George Sampson's excellent three-volume edition of Berkeley's writings (London, 1897-8), or

So, too, Bernard de Mandeville—a physician and a son of a physician, a student of Rotterdam, a graduate of Leyden in 1689, and a practicioner come upon evil days in London. An early advocate of the Cartesian theory of automatism among animals, a stimulating essayist upon "Hypochondria" and an opponent of speculative therapeutics—Mandeville became famous, or infamous, as the author of "The Fable of the Bees"—an ingenious political satire of the state of England in 1705, whose philosophic half-truths gave Adam Smith the germ of his doctrine of self-interest as the dominant motive of socio-economic action, and perhaps even paved the way for nineteenth century utilitarianism.[6]

Of this goodly company[7] I have selected two worthies for somewhat closer notice—Sir William Petty and François Quesnay. In the history of medicine the position of each is at least respectable. In the history of economics, it is distinguished. Petty, if not, as he has been called,[8] "the founder of political economy"—was the first to insist that economic facts must be studied by the precise methods of physical science, and to that end fashioned the device of "political arithmetic." Quesnay, the author of the "Tableau Economique"—which the elder Mirabeau grouped with the alphabet and money as the three great inventions of the human mind—was the master of the first real school of political economists, the *économistes* or physiocrats of pre-revolutionary France. Finally, each figured appreciably in the history of his time. Petty was the director of the Down Survey of Ireland, and became the progenitor of the Lansdowne family. Quesnay was the trusted physician of Madame de Pompadour and an influential court figure in the closing decades of the *Ancien Régime*.

The facts of Petty's life, long familiar in essential, have been elaborated in recent years by his lineal descendant, Lord Edmond Fitzmaurice, with the aid of family archives, and it is of this record that liberal use has been made in the following paragraphs.[9] Born at Rumsey, in Hampshire, in 1623, the son of Anthony Petty, of whom Aubrey states that "by profession he was a clothier, and also did dye his own cloths," Petty received the usual school education, including "a competent smattering" of Latin and Greek, but mitigated by contact in leisure hours with the trades and crafts of the neighborhood. Chafing under home restraint, Petty at fifteen bound himself apprentice to the master of a sailing vessel. The experience was short and painful. He was ill-treated at sea, and finally left stranded with a broken leg at a small inn on the French coast near Caen—perhaps his first grim acquaintance with the opportunities of surgical skill. His plight excited the sympathy of the neighborhood, and his precocity won friends and patrons. Abandoning the sea, he entered a private school, and later the Jesuit College at Caen, the Fathers consenting to take the young Englishman as a pupil with the condition "that their attempts on his religion should be confined to prayers for his conversion."[10]

After leaving the college at Caen, young Petty entered the Royal Navy; but at the outbreak of the Civil War he retired to the continent, not to return to England until three years later, in 1646. These three *Wanderjahre* were spent in France and in the Netherlands. At Utrecht, Leyden, Amsterdam and later at Paris his interest, converging upon the physical and mathematical sciences, eventually concentrated upon anatomy. In Paris he met Hobbes, and Aubrey records that they read Vesalius together. These were rare days in France. The spirit of scientific inquiry was in the air and the old limits upon human knowledge seemed passed.

Returning to England in 1646, Petty, then twenty-three, was driven less by preference than by lack of other opportunity to recur to his father's business. Other projects engaged his leisure—an invention for double writing, a college of tradesmen, and the design of a history of trade. But an even more ambitious intention was forming. "A most rare and exact anatomist," wrote Hartlib of Petty to Boyle, and Petty himself records, "I intend, God willing, so soone as possibly I can, to take the degree of Dr. of Physicke," adding comfortably, "which being done, it will bee a discredit for mee and consequently a great hindrance to mee, to goe and buy small matters, and to doe other triviall businesses."[11]

Petty enjoyed the friendship of influential supporters of the Protector, and in due course was created a fellow of Brasenose. The appointment was variously justified as made because "of his rare qualities and gifts," because "he had cut up Dogges and taught anatomy in the war," and somewhat spitefully, because the visitors "liked to put out loyal persons in order to put him and such others in." With the fellowship came appointment as Deputy to the University Professor of Anatomy, Dr. Clayton—whose efficiency was apparently impaired by "an insurmountable aversion to the sight of a mangled corpse." The reinforcement was admirable. "Anatomy"—Aubrey reports—"was then little understood by the University and I recollect that Dr. Petty kept a body that he brought by water from Reading, a good while to read on, some way preserved or pickled."

more conveniently in the reprint which I have edited (Baltimore, 1910) with the title-pages of the original edition reproduced in facsimile and the original pagination indicated.

[6] Mandeville's economic philosophy is discussed in James Bonar, "Philosophy and Political Economy" (London, 1893), passim, in Leslie Stephen, "History of English Thought in the Eighteenth Century" (second ed., New York, 1881) chap. IX, sect. iii, in Edwin Cannan (ed.), "Adam Smith's Wealth of Nations" (London, 1904), xliii-xlvi and in "Dictionary of Political Economy" (ed. Palgrave), *sub nom.*

[7] I am indebted to Dr. William H. Welch for the happy reminder that mention should at least be made of Copernicus, who, on the one hand, pursued medical studies at Padua and engaged in active practice at Frauenburg, and who, on the other hand, presented a scheme for the reform of the Prussian Polish currency in a treatise, "De monetae cudendae ratione," which Wolowski made accessible in 1864 in conjunction with the currency tract of Nicole Oresme.

[8] Lord Edmond Fitzmaurice in "Dictionary of Political Economy" (ed. Palgrave) *sub* "Petty."

[9] A sketch of Petty, based upon Fitzmaurice, appeared in the *British Medical Journal*, June 11, 1898, pp. 1529-1531, under the caption, "Lord Lansdowne's Medical Ancestor."

[10] Fitzmaurice, p. 3.

[11] Fitzmaurice, p. 14.

But the circumstance which established Petty's medical fame throughout the country-side, is associated neither with class-room nor clinic. The particulars, as detailed by Fitzmaurice, are curious enough to warrant citation in full: [12]

> One Ann Green had been tried, convicted, and executed at Oxford on December 14, 1651, for the murder of her illegitimate child. Her execution seems to have been carried out with a combination of clumsiness and brutality characteristic of the times. It was observed "by the spectators that she seemed to take an unconscionable time in dying, so her friends went to assist her in getting out of this world, some of them thumping her on the breast, others hanging with all their weight upon her legs, sometimes lifting her up and then pulling her down again with a sudden jerk." At length the Sheriff was satisfied, and the unfortunate woman was certified to be dead. The body was then cut down, put into a coffin, and taken to the dissecting room. When, however, the coffin lid was opened she was seen to be still breathing and to "rattle," "which being observed by a lusty fellow who stood by, he, thinking to do an act of charity in ridding her out of the reliques of a painful life, stamped several times on her breast and stomach with all the force he could." Just at this moment, however, Dr. Petty and Dr. Wilkins appeared on the scene, and recognising distinct signs of life, decided to attempt to revive the supposed corpse. They wrenched open Ann Green's teeth, poured cordials down her throat, and persuaded a woman to go to bed with her to restore warmth. Signs of life soon began to appear; the doctors bled her, ordered her a julep, and so left her for the night. In two hours she began to talk. The dead had come to life. Though legally defunct, she is said to have survived to marry and become the mother of children, in spite of the Sheriff and to the confusion of the hangman.

Soon after this event, perhaps in consequence of it, Petty was made vice-principal of Brasenose and succeeded to the chair of anatomy. Further academic distinction followed—the professorship of music at Gresham College—a less bizarre association in the days when the quadrivium was still an academic tradition, than in our own times.

The residence in Oxford repeated in major scale the stimulating contacts of his Paris sojourn. A notable group interested in chemico-medical studies had gathered there in refuge from the stress of civil disorder, and we are told that: "In these stormy times they used, for the convenience of inspecting drugs, to meet at Dr. Petty's lodgings at an apothecary's house, as he was acknowledged to bear away the palm from all competitors in the experimental side of natural philosophy." [13]

In 1651 Petty obtained a two years' leave of absence, with the intention perhaps of further travel and study on the continent. But this plan was abruptly changed and the whole subsequent course of his life fashioned by his appointment as physician-general to the army in Ireland.

In this capacity Petty reorganized the medical service of the army, "reducing that affair," as he claimed, "to a state of easiness and plainness which before was held a mystery, and the vexation of such as laboured to administer it well." Opportunities for private study were not lacking. Robert Boyle described how, "in the course of experiments in anatomy, which they at this time carried out together, he had satisfied himself of the circulation of the blood, and the freshly discovered *receptaculum chyli*, made by the influence of the *venae lactae;* and had seen especially in the dissection of fishes, more of the variety of the contrivances of Nature and the majesty and wisdom of her author, than all the books he ever read in his life could give him convincing notions of." [14]

But the activities of Petty as physician were drawing to an end, and his career as economist and economic administrator opening up. The determining circumstance was his selection by the government to conduct a survey of Ireland, preliminary to the allotment of forfeited lands among the troops, after the suppression of the insurrection. Petty received large tracts in payment for his services, and this, together with judicious purchases, laid the basis of the family fortune. Much of his energy was thereafter absorbed in defending his land titles and in managing his extensive property.

Returning to London, Petty associated with a group of followers of the new philosophy and was instrumental in founding the Royal Society in 1662, and became a charter member of its council. He was one of the charter fellows of the College of Physicians in Dublin and aided in founding the Dublin Philosophical Society, to whose proceedings he contributed various papers. He was knighted in 1662 upon the incorporation of the Royal Society and died in London in 1678. "If I were a prince, I should make him my second counsellor at least," was Evelyn's estimate, while Pepys added he was "the most rational man that ever I heard speak with a tongue."

Petty's economic writings represent the literary productivity of the last twenty-five years of his life. They are still obtainable in original editions, though rare; but they have been made accessible in an admirable reprint edited with scholarly apparatus by Professor Hull of Cornell University and published in 1899 by the Cambridge University Press.

These writings are all more or less directly associated with Petty's residence in Ireland and the resulting political intercourse. They were not "conscious elaborations of some economic system, more or less clearly conceived," but "each of them, on the contrary, was prompted by some circumstance of the times, and addresses itself, in fact if not in form, to some question of the day." [15] Thus the "Treatise of Taxes and Contributions"—the earliest and most systematic of Petty's economic writings—grew out of the changes in the revenue which the Restoration occasioned. The "Verbum Sapienti" is due to the costliness of the recoinage project of Halifax. The various essays in "Political Arithmetick" were probably animated by the purpose of establishing the great strength of London as against Paris. The studies of the "Dublin Bills of Mortality," the "Treatise of Ireland" and the "Political Anatomy of Ireland" represented the direct use of materials collected in or suggested by his interest in Ireland.

How much Petty the economist was influenced by Petty the physician appears in the title "The Political Anatomy of Ire-

[12] Fitzmaurice, pp. 18-19; based upon the contemporary account "News from the Dead" (Oxford, 1651), described by Hull in "Works," xv. The incident actually occurred in 1650.

[13] Fitzmaurice, p. 20.

[14] Fitzmaurice, p. 22.

[15] Hull, lxi.

land "[16]—a manner of natural history of the island, suggested by Chamberlayne's "Angliae Notitia"—and even more in the preface to the book:

> Sir Francis Bacon, in his Advancement of Learning, hath made a judicious Parallel in many particulars, between the Body Natural, and Body Politick, and between the Arts of preserving both in Health and Strength: And it is as reasonable, that as Anatomy is the best foundation of one, so also of the other; and that to practice upon the Politick, without knowing the Symmetry, Fabrick, and Proportion of it, is as casual as the practice of Old-women and Empyricks.
>
> Now, because Anatomy is not only necessary in Physicians, but laudable in every Philosophical person whatsoever; I therefore, who profess no Politicks, have, for my curiosity, at large attempted the first Essay of Political Anatomy.
>
> Furthermore, as Students in Medicine, practice their inquiries upon cheap and common Animals, and such whose actions they are best acquainted with, and where there is the least confusion and perplexure of Parts; I have chosen Ireland as such a Political Animal, who is scarce Twenty years old; where the Intrigue of State is not very complicate, and with which I have been conversant from an Embrion; and in which, if I have done amiss, the fault may be easily mended by another.
>
> 'Tis true, that curious Dissections cannot be made without variety of proper Instruménts; whereas I have had only a commin Knife and a Clout, instead of the many more helps which such a Work requires: However, my rude approaches being enough to find whereabout the Liver and Spleen, and Lungs lye, tho' not to discern the Lymphatick Vessels, the Plexus, Choroidus, the Volvuli of vessels within the Testicles; yet not knowing, that even what I have here readily done, was much considered, or indeed thought useful by others, I have ventur'd to begin a new Work, which, when Corrected and Enlarged by better Hands and Helps, I believe will tend to the Peace and Plenty of my Country; besides which, I have no other end.

It is to Petty's studies in "political arithmetic," however, that the historian of economic science ascribes the largest importance. There are interesting doctrinal contributions in the papers on currency and taxation; but the quasi-statistical studies possess a more general significance. Petty, as we have noted, was one of the group of experimental investigators, working in the spirit of the "Novum Organum" who began the systematic pursuit of scientific knowledge in England. When economic problems forced themselves upon his attention, it was inevitable that Petty should attempt their solution by the same scientific methods and with the same fundamental assumptions—the uniformity of law, quantitative precision, experimental test—that had figured in his earlier studies in medicine and in mechanics.

To economic study, pursued in this spirit, Petty gave the name "political arithmetic"—a beginning of what is now called statistics, but differing therefrom in that it undertook to reach conclusions upon matters as to which available data were much too inadequate to permit generalizations by bare statistical inference. Thus Graunt and not Petty is recognized as the founder of statistical science, because limiting his inquiry to the bills of mortality—the one field in which a considerable body of enumerated facts was at that time available—Graunt laid the basis of such study both in method and result.

Petty's studies, on the other hand, in giving wider extension to this method—even involving extravagant, almost ludicrous, exploitation of insufficient data—first emphasized the need and stimulated the collection of economic facts. For almost a century, political arithmetic continued to be regarded as the device whereby economic principles could be formulated. After the labors of David Hume and Adam Smith had definitely established political economy as a form of social philosophy, political arithmetic lapsèd definitely into an outgrown creed. Thereafter none too unworthy to cast a stone:

> Hail! most prudent Politicians,
> Hail! correct Arithmeticians,

jeered the Rolliad in 1785. A few year later the "new-coined name" of statistics crept unobtrusively into England, and in 1801, with the definite returns of the first census, all possibility of political arithmetic serving as a technical economic method came to an end.

None of Petty's medical writings are accessible. None were ever published (with the bare exception of an abstract of a paper on mineral waters contributed to the Dublin Philosophical Society), and our only clue is a list of his works left by Petty himself and reprinted both by Fitzmaurice and by Hull. The medical entries are as follows:

1645 (Holland). An History of Seven Months Practice in a Chemical Laboratory.
1646 (Paris and Oxford). A Discourse in Latin, "de Arthritide et Lue Venerea"; and "Cursus Anatomicus."
1649 (Oxford). Six Phisico-Medicall Lectures, read at Oxford.
1650 (London). Three Osteological Lectures.
1651 (London). Collection of Experiments.
1652 (London). Pharmacopœa and formula Medicamentorum.
1652 (London). Observationes Medicæ et Praxis.
1653 (Ireland). De Plantis. Notæ in Hippocratem.

It is possible that certain of these are preserved among the Petty MSS. in the possession of the Lansdowne family at Bowood. Such is certainly the case with his inaugural lecture as professor of anatomy at Oxford on the growth and present position of medicine, from the MS. notes of which Lord Fitzmaurice quotes a tantalizing paragraph. As to the other items he gives no hint, while Professor Hull, whose opinion is peculiarly competent, writes me:

> To my great regret I do not know anything of Petty's medical writings, indeed I never knew more of them than appears in the bibliography in Vol. II of his writings, which does not seem to indicate that any of them were printed. The Hester Anna Green pamphlet is probably not by him, and is scarcely medical in any event. To the best of my recollection I could find nothing detailed on his medical or anatomical performances.

It would be an extremely useful service if some student in this company, interested in the history of medicine, should undertake, perhaps in the course of a visit to England at some more propitious time, to determine this uncertainty, and even—if the event make it possible—to compile a précis or calendar of Petty's medical papers.

[16] [1672] London, 1691.

Far less chequered and eventful is the life of François Quesnay. Born at Méré near Versailles in 1694, the son of an advocate and landed proprietor of modest circumstances, Quesnay's childhood was spent in deliberate neglect of formal instruction, curiously anticipating Rousseau's doctrine that it is best to strengthen the body before wearying the mind. Up to his eleventh year he was unable even to read, while, on the other hand, the life of the fields and the habits of the countryside entered into his very being.

Once supplied with books, the mental pace was rapid. Natural science—botany, physics, chemistry, mathematics—and, above all, medicine attracted him. At sixteen he was apprenticed to a local surgeon, passing thence to Paris for more systematic study. In due course he qualified as a master surgeon and settled down to practice at Mantes. His life here was that of a hard-working country physician, gaining the confidence of his community, winning appointment in the hospital at Mantes, and adding to his store of experience.

His practice extended to the chateaus of the neighborhood and led to acquaintance with the Maréchal de Noailles. The acquaintance ripened into regard and friendship, opening up influential avenues of acquaintance, even to presentation to the Queen, by whom he was thereafter summoned whenever she visited Maintenon.

Quesnay first attracted notice by the publication in 1730 of a tract in criticism of a treatise on bleeding written by Silva, then head of the medical profession of Paris. At first ignored as a presumptuous impertinence, the validity of the critique "founded upon the laws of hydrostatics" was admitted, and the modest surgeon of Mantes entered the medical world of Paris.

With Noailles as sponsor, Quesnay was introduced to La Peyronnie, first physician-surgeon of the King. Peyronnie, in the hope of elevating the practice of surgery, then separated from medicine and often associated with the art of the hairdresser, had in 1731 obtained the establishment of the Academy of Surgery. He recognized in Quesnay a valuable acquisition and attached him to the new institution in the capacity of perpetual secretary, after having secured for him the appointment of surgeon-ordinary of the King. Quesnay was installed in the household of the Duke of Villeroi as physician and the way opened for distinction and reward.

Madame de Pompadour bestowed the grace of her patronage, and Quesnay became in turn first physician-ordinary and first physician-consultant of the King. The King himself found enough profit in Quesnay's company to call him familiarly "mon penseur," probably, as Mr. Higgs observes,[17] a play upon words—the French verb *panser,* to give medical and especially surgical assistance, lending itself to a pun upon *penser,* just as a blood-letting barber was styled "*le seigneur* (saigneur) *barbier.*" In any event Louis mitigated the jest by conferring letters of nobility upon Quesnay and selecting in person his arms—three pansies—and the device "propter cogitationem mentis."

[17] Higgs "Physiocrats," Appendix, Note A.

At a time when opportunity and intrigue rather than merit and virtue made men and determined careers, it is not surprising to find a more picturesque explanation of Quesnay's rise. Lord Crawford, the earliest editor of the memoirs of Madame du Hausset, lady-in-waiting of Pompadour, tells the story:[18] The Countess d'Estrades, then the favorite of Pompadour, while receiving a visit from the Duke of Villeroi was taken with sudden indisposition. Villeroi hurriedly called his physician, Quesnay, whom he had left waiting in his carriage. Recognizing that the Countess was subject to epilepsy and that she was on the verge of an attack, Quesnay with admirable discretion reassured Villeroi, ordered sedatives, dismissed the company with the explanation of "nerves," and then ministered to the unfortunate lady. The Countess—consciousness regained—realized her debt. She spoke to her mistress Pompadour of Quesnay's skill and discretion, with the result that Madame took him as her own physician, gave him apartments adjoining her own at Versailles and obtained for him the appointment of "médecin ordinaire du roi."

From the publication of the critique of Silva in 1730, Quesnay's scientific activity was marked. As secretary of the Academy of Surgery, he not only edited the memoirs of the society, contributing papers and prefaces thereto, but bore the brunt of the acrimonious controversy which the faculty of medicine waged for seven years against the new Academy of Surgery to determine the respective provinces of the two professions.

Unlike Petty, Quesnay published his medical writings and had the satisfaction of seeing them enjoy wide circulation and successive edition. The Surgeon-General's Library contains practically all of the texts—indeed some whose authorship is not beyond doubt—and intelligent summaries are found in Oncken's edition of the "economic and philosophical" works. There have also been various appreciations of Quesnay's work within the medical profession itself:[19] M. Bouisson read a memoir upon Quesnay under the title of "Un Chirurgien-Economiste" before the faculty of medicine of Monpellier in 1879. M. Ferrand contributed a paper on the medical work of Quesnay to the Paris Bulletin de l'Académie de Médecine in 1896. Cabanes has a gossipy chapter on "Le Médicin de Madame de Pompadour" in his "Cabinet Secret de l'Histoire" (1897). A brief unsigned feuilleton on "Franz Quesnay, Leibarzt Ludwig XV," appeared in the Deutsche Medicinische Wochenschrift in 1901.

In order of publication the more important works are as follows:

Observations sur les effets de la saignée . . . . (Paris, 1730).
Histoire de l'origine et des progrès de la chirurgie en France (Paris, 1744).
Traité de la gangrène (Paris, 1749).
Traité de la suppuration (Paris, 1749).
Traité des effets et de l'usage de la saignée . . . . (Paris, 1750).
Traité des fièvres continues . . . . (Paris, 1753).

[18] Oncken, p. 115 n.

[19] Index Catalogues of the Library of the Surgeon-General's Office, *sub* "Quesnay."

The "Treatise on Fevers," published in 1753, was the last of Quesnay's medical writings. Then in his sixtieth year, driven by weakened eyesight to forego surgical practice, this stoppage might well be accounted the inevitable advent of intellectual dulness. As a matter of fact, it marked the beginning of his larger service. Just as Petty the anatomist yielded to Petty the political arithmetician, so Quesnay the court-physician was succeeded by Quesnay the political economist. It is a curious coincidence that an exact hundred years separates the turning points. But with this the parallel ends. Petty was but thirty when the change came, with almost as many of his best years still before him; Quesnay had reached his sixtieth year with the inevitable end almost in sight. It is possible, too, to lay finger upon the precise events responsible for Petty's transition. In the case of Quesnay, this is far from clear and commentators diverge widely in their opinion. Garnier contends that Quesnay's study of the physiology of the human body tended to direct his attention to the physiology of the social body, and to the search for those uniformities which might be expected to prevail in social and economic relations. Higgs maintains that Quesnay's economic studies were inspired by Richard Cantillon's "Essay upon the Nature of Commerce," published in 1755, and that the school of the physiocrats dates from the interview in July, 1757, of Quesnay and Mirabeau. Oncken and Weulersse, making profounder analysis, call attention to the increasing restlessness of French philosophical writers of the early eighteenth century as to the economic abuses and financial ills of the kingdom, finding expression in the burst of independent thought which followed the Peace of Aix-la-Chapelle in 1748.

It is likely that the real explanation involves some part of each of these opinions. From early childhood Quesnay had seen the nourishing richness of Mother Earth, and the desperate poverty of those who cultivated her. Paris and Versailles rounded out the contrast—an industrious artisan class eking out a bare existence and a parasitic court drawing a golden fund from land ownership only to squander it in wanton excess. Obviously, it was distribution, not production, that wrought the poverty of the nation. Nature was bounteous, but the apportionment was at fault.

The initial task was to ascertain the principles governing the distribution or "circulation" of wealth. The conviction that there must be such uniformities or laws was an inevitable heritage from Quesnay's interest in natural science—a phase of that same enthusiastic endeavor to formulate principles of economic action which Montesquieu's "Spirit of Laws" represented in France, and David Hume's "Moral and Political Essays" embodied in England.

Quesnay's earliest economic writings were two articles on "Farmers" and "Cereals," contributed in 1755-6 to the *Encyclopédie* of Diderot and D'Alembert. The first presents an intelligent discussion of agricultural conditions in France, but contains little of theoretical importance. In the second article, "Cereals," we have a much more significant exposition of Quesnay's views. The essay sets forth that the true economic policy of France was not to stimulate manufactures, but to develop the great productive powers of the soil. Agriculture is the real and the only source of national wealth. Farming is the true basis of prosperity and the rent of the landlord is the source from which public taxes should be paid. Free trade in commerce and laissez-faire in industry are essential to national well-being. The essay concludes with fourteen maxims of government, summarizing these arguments into a programme of practical reform.

In 1756 Mirabeau published his "L'Ami des Hommes." In essence, a commentary upon Cantillon's neglected essay, the work gave circulation and vogue to economic liberalism. The author became the popular idol, and the book ran through forty editions. In scholarly circles, too, there was response. Quesnay read the book and was stirred by it. A personal meeting followed, Quesnay expounded his own philosophy, with the result that Mirabeau became an ardent disciple and Quesnay agreed to attempt a precise formulation of doctrines.

The resulting performance was the "Tableau Oeconomique"—the *tour de force* upon which Quesnay's fame as an economist rests, and a work of some moment in the general history of literature. The circumstances surrounding its publication are in themselves of interest.[20] "The tactful Pompadour" persuaded Quesnay to forego his intention of public issue, and, in lieu thereof, to print it privately at Versailles in December, 1758. Only a few proofs were struck off, and it was long supposed that all of these were lost, the Tableau itself being available only as incorporated in later writings. In 1890, however, Dr. Stephen Bauer discovered among the manuscripts of Mirabeau in the Archives Nationales at Paris, a copy of the Tableau slightly revised by Quesnay himself, and this copy was reproduced in facsimile by the British Economic Association in honor of Quesnay's bicentenary in 1894.

The Tableau proper is a chart or graph covering a quarto page and designed to show visually the results of agricultural production. Starting out with the assumption of six hundred livres a year devoted to agriculture, the Tableau traces the circulation and partition of this among various economic classes to the end of locating the social surplus. In the matter of rapid intelligibility, the chart has been conservatively described as "a ludicrous failure." Francis Horner records that the Earl of Lauderdale, a distinguished economic writer of the pre-Ricardian period, never left the accursed zigzag without evaluating himself as a block-head, and to later students it stands alone—or, at most, associated with John Stuart Mill's "fourth fundamental proposition concerning capital"—as the *pons asinorum* of economic exposition.

What Quesnay meant that the Tableau should make clear, and what to the brilliant coterie that speedily gathered about him, it apparently established was: Agriculture alone is the source of national wealth. Whereas industry and commerce are sterile, at best yielding enough to replace the labor and capital involved therein, the cultivation of the soil yields a net product. Inasmuch as this *produit net* is the only true national revenue, so should it be the only object of taxation.

[20] Higgs, p. 42.

The state should be supported by a single, direct tax or *impôt unique* levied upon land. Finally, there should be no interference of any kind on the part of the state with the activities of individuals engaged in the production and circulation of wealth.

Quesnay's remaining economic writings took the form of contributions to the "Journal of Agriculture" and the "Ephemerides"—organs of the sect. He later reverted to mathematical studies, and in his old age he came to believe that he had solved the problem of squaring the circle. With the death of Louis XV, Quesnay lost court favor, and he died at Versailles on December 16, 1774.

Quesnay's doctrines were developed and popularized by a remarkable group of philosophers and savants, styling themselves "the economists," but better known in J. B. Say's phrase as "the physiocrats"—Mirabeau, Du Pont de Nemours, Mercière de la Rivière, Baudeau, Le Trosne, and Saint-Peravy. Gathered in disciple-like veneration about their sage, this gifted group constitute the unique example of an economic school or sect in the history of the science. By meetings, by journals and by writings, its members spread the doctrines of physiocracy over France and over Europe. In the world of affairs, the influence made for economic freedom, for simplification of taxation, for encouragement of productive effort. In the world of thought, the contributions were recognition of economic uniformities, enthusiasm for economic study, and emphasis upon laws of economic distribution. The specific doctrines were ultimately discarded. The practical proposals were rejected. But the larger service endured. It was in something more than fraternal regard, in almost a scholar's prescience that Adam Smith conceived the purpose of inscribing the "Wealth of Nations" to the "very ingenious and profound author," the "modest and simple" founder of the physiocratic school.

DISCUSSION.

DR. WELCH: Dr. Hollander has done us a great service in giving us this beautiful presentation of the subject. It is a very valuable contribution.

It is very interesting to consider physicians who became distinguished in other branches of knowledge. I have myself been more or less interested in this subject, considering, for instance, physicians who have been classic scholars, physicians who have been astronomers, etc. It is not difficult to find physicians who are eminent in the natural sciences. Dr. Kelly, for instance, has brought out the physicians who have been botanists. There have also been zoologists. This is all more or less familiar ground. It is much less common to find those eminent in physical sciences, but still the list is interesting and considerable. Those who have become eminent in the social sciences are relatively few. I rather think this is due to the fact that medicine had become pretty highly specialized by the time the social sciences were developed. The points Dr. Hollander brought out as to the relationship between medicine and the social sciences were extremely interesting. So also is his list of physicians. I think there is perhaps one name that might be added—that of Copernicus, with his essay on money. He was educated in medicine and actually practised it.

The two names selected for special consideration—Petty and Quesnay—are of course very different. Each was the child of his time and a very good example. Petty belongs to the group of men at Oxford and later at London developing the so-called new philosophy, himself the very heart of that group and one of the founders of the Royal Society. But no less so Quesnay, the child of the so-called philosophical century, and the chief representative in medicine among the encyclopedists, as they were named.

The relation of Petty to Graunt is very interesting. Graunt is doubtless the founder of the science of vital statistics. His materials were the bills of mortality collected in the hands of the parish clerks. This was an ecclesiastical function and it remained in the hands of the parish clerks until 1836, when the Birth and Death Registration Act was passed. It is very interesting to consider the influence which the analysis of the bills of mortality—that is, the returns and registration of births, marriages and deaths—has had upon the development of preventive medicine. Petty and Graunt were most interested in its practical bearings. Edmund Halley, a contemporary of Sir Isaac Newton, collected the Breslau tables. Süssmilch is regarded as one of the modern founders of statistics, but the practical application of the knowledge thus derived was really made in England partly in the eighteenth and partly in the early part of the nineteenth century.

It is interesting to note that some of the English physicians took local analyses in the towns in which they lived, going around on their own initiative and taking a census. There was even a questionnaire of seven questions, and from that they drew conclusions as to the importance of isolating cases of infectious disease, etc. It was in 1836 that the famous Birth and Death Registration Act was passed and the Registrar General's office established, twelve years before the Public Health Act of 1848. It was from the data collected by the Registrar General during these earlier years that these practical measures in hygiene and preventive medicine were introduced in England. In this connection one name should never be forgotten, that of Dr. William Farr, who was connected for over forty years with the work of the Registrar's office, and who is in many ways the most important and interesting in the whole domain of vital statistics. His letters published in the reports of the Registrar General are of course classics.

Quesnay is really an interesting character in medicine as well as in economics. He was a much more highly educated surgeon than most of his day and was really the spokesman of the surgeons after the establishment of the Academy of Surgery. One of the most acrimonious controversies in the whole history of medicine, and the most discreditable in many ways, took place in regard to the establishment of the Academy of Surgery. The Academy of Medicine wanted to keep the surgeons back in every way, but finally they succeeded in getting the royal assent to the establishment of the Academy of Surgery. Quesnay was the second secretary. He it was who edited the Memoirs. His preface to the first volume is well worth reading. It is rather interesting to consider who was the champion on the other side. His is a name that started a line of thought and investigation and is as famous perhaps as Quesnay's. Astruc was the Professor of Medicine in the Faculty of Medicine when Quesnay was the secretary of the Academy of Surgery. Astruc is best known in medicine by his two great volumes on the venereal diseases, which still have much historical interest. It was Astruc who discovered the two sources or documents in the Pentateuch—the distinction between the Eloistic and Jeovistic writings. This work opened the path for all the later higher Biblical criticism. It is interesting that on the one hand we have Quesnay, the surgeon, as a contributor to economics, and on the other his great opponent, Astruc, identified with the first important work in the so-called higher criticism of the Bible—his famous conjectures on the sources which Moses had at his disposal for writing the Book of Genesis.

I have brought here the familiar translation by Otley of some of Quesnay's writings. His remarks on wounds of the brain are most interesting, with his plea for careful surgical intervention

in diseases of the brain, based upon an analysis of cases that came to post-mortem examination.

DR. GARRISON: Nothing, of course, could be added to the subject which Dr. Hollander has so admirably presented. We came over to be instructed and have learned a great deal. I have two books with me which may have some interest. One is the fourth impression of John Graunt's "Natural and Political Observations" (1665), which throws considerable light on the origin of vital statistics in England. Mr. Froude begins his History of England (Reformation period) with the observation that the growth of the population at that time was very slow, on account of the wars, epidemics, etc. All through the sixteenth century there was practically no increase. John Graunt says that "Bills of Mortality" were first made in 1592 and resumed in 1603, and that "the rise of keeping these Accompts was taken from the Plague." He gives a very curious account of the method of gathering vital statistics:

"10. We have hitherto described the several steps whereby the *Bills* of *Mortality* are come up to their present state; we come next to shew how they are made, and composed, which is in this manner, *viz.:* When any one dies, then, either by tolling, or ringing of a Bell, or by bespeaking of a Grave of the *Sexton*, the same is known to the *Searchers*, corresponding with the said *Sexton*.

"11. The *Searchers* hereupon (who are ancient Matrons, sworn to their Office) repair to the place, where the dead Corps lies, and by view of the same, and by other enquiries, they examine by what *Disease* or *Casualty* the Corps died. Hereupon they make their Report to the *Parish-Clerk*, and he, every *Tuesday*-night, carries in an Accompt of all the *Burials* and *Christnings*, happening that Week to the *Clerk* of the *Hall*. On *Wednesday* the general Accompt is made up, and Printed, and on *Thursday* published, and dispersed to the several Families, who will pay four Shilling *per Annum* for them."

Graunt's book is very gossipy and entertaining as to the different medical statistics taken. His synopsis of contents and his observations show him to have been a man of untrained mind with a clever capacity for shrewd observation here and there, suggesting some one thinking aloud.

The other book is the second edition of "Die göttliche Ordnung in denen Veränderungen des menschlichen Geschlechts" of Süssmilch (1742), the most important work on vital statistics in the eighteenth century. It is said that the merits of Süssmilch are that he obtained better results than Petty and Graunt by using larger figures. Perhaps he came to that in this way: Early in the eighteenth century, there came to England one Abraham de Moivre, a mathematician and refugee from France, who was driven out by the revocation of the Edict of Nantes. At that time, gaming was very common in England and a gambling debt was accounted a debt of honor, to be paid before grocers', tailors' or other tradesmen's bills. A great interest was thus taken in the doctrine of chances, *e. g.*, the probability of any facet of a die turning up in a given number of throws. De Moivre is said to have made his living by solving problems of this kind for gamesters in a tavern in St. Martin's Lane. In 1716 he published his "Doctrine of Chances," which states most of the theorems between Pascal and La Place. In vital statistics, as in dice throwing, the probability of occurrence and recurrence is the more constant the greater the number of chances. With this knowledge, Süssmilch got better statistical results than his predecessors, and by applying Deparcieux's idea of "mean expectation of life" (1746), he made the first life table (1746), which was used in Germany all through the eighteenth century for actuarial calculations.

COMMON ORGANISMS IN HEATED MILK: THEIR RELATION TO ITS REACTIONS.

By L. P. SHIPPEN, M. D.

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The organisms surviving in milk after heating at various temperatures have an especial interest on account of the importance attached to pasteurization. Flügge[1] in Germany, and Ford and Pryor[2] in this country have shown that the spore-bearing group is very resistant, and Ayers and Johnson[3] and other observers have found that in milk heated to and kept for a certain time at temperatures ranging from 60 to 75° C. there exist, in addition, many varieties of non-sporulating bacteria. In the following paper an attempt has been made to identify the most common of these organisms, to ascertain roughly the temperatures at which they are recovered, and to observe what relation they bear to the reactions of the milk in which they occur.

For this purpose, milk was obtained from the stores in the vicinity in sterile flasks and was transferred in the laboratory to sterile test tubes, especial care being taken not to allow any milk to come in contact with the cotton plugs. The tubes were then placed in a water-bath previously raised to the required temperature, and held at 60, 65, 70, 80 and 85° C. for 15 minutes, after which they were plunged into cold water for five minutes. By this method the milk was kept at the desired temperature for from ten to thirteen minutes, as control tubes showed that it required from two to five minutes for the milk to assume the heat of the water-bath.

These tubes were incubated for two days and at the end of the first and second days the milk was plated upon plain agar and upon dextrose agar. The plates were studied after two days' incubation, and their colonies transferred to slant agar and to milk. Whenever necessary, plating was again resorted to, in order to purify the cultures. No attempt was made to isolate organisms whose growth was so slow that their colonies did not appear until after two days' incubation, for it was felt that such bacteria could have very little relation to the comparatively rapid reactions occurring in heated milk.

The 60° milk, after one day's incubation, sometimes showed little change, sometimes was coagulated and at other times peptonized. In from two to four days peptonization was often complete, but quite as frequently only coagulation with the production of whey and acidity occurred. The reactions were very inconstant, ranging from a normal clotting to complete peptonization; and test tubes taken from one sample of milk often showed as wide variations as the test tubes from different

specimens. No gas formation was ever observed, nor did transfers to dextrose broth produce any gas. In this the observations of the writer are not in accord with those of Ford and Pryor, who found that milk heated to 60° C. often showed a violent gas production. This divergence may be explained by a consideration of the different conditions under which the experiments were made. In the cases in which gas was observed the workers used flasks of milk, in which anaërobic conditions prevailed, so that the anaërobic gas producers were enabled to produce some effect upon the milk. In our experiments, in which no gas formation was observed, test-tubes were substituted for the flasks, and in these aërobic conditions alone existed.

Plates of plain agar made from the milk after one and two days' incubation showed a bacteriological finding as inconstant as the reactions, and seemingly bore little relation to the coagulation or peptonization of the milk. In some cases the peptonized milk was found to contain few spore-bearing varieties, whereas in coagulated milk after one day's incubation the spore-bearers sometimes seemed to be the predominant species.

Various strains of *Streptococcus lacticus* were isolated in every instance. This organism is more properly termed *Bact. güntherii*, as has been noted in a previous article,[4] but the name *Streptococcus lacticus* having been generally adopted the writer in this paper prefers to use the latter appellation. Usually it possesses the power of firmly and quickly coagulating milk, but many strains merely produce a slight acidity even after a week or more in the thermostat. The majority of cultures isolated from the 60° milk belonged to this latter type, although occasionally a strain was picked up which retained the power of rapid coagulation. However, in the experience of the writer, some strains of *Str. lact.*, which have very little effect on milk when inoculated by means of the platinum wire, may firmly clot this medium when vastly greater numbers are transferred. Thus, a tube of sterile milk may become firmly coagulated 24 hours after being poured upon an agar slant culture of a strain of *Str. lact.*, which had merely a slight acid-forming power when transferred to milk in the usual fashion. The organism was recovered both from coagulated and peptonized specimens and frequently in both cases, after the milk had been incubated for two days, was found to have overgrown the other species so that the plates of greatest dilution contained only this bacterium. When dextrose agar was used for plating the colonies were even more numerous, but when transferred to plain agar many of these refused to grow. When transferred directly to milk some of these strains coagulated this medium in a typical manner; others, like the majority of those growing on plain agar, merely produced a slight acidity.

The organism next most frequently encountered in the milk heated to 60° C. closely resembled a species previously identified[4] as *Bact. troilii* (*Bact. lactis longi b*, Matzuschita). This organism is a short, gram positive bacterium, without motility, whose cultural reactions are similar to those of *B. fecalis alkaligenes*. The strains isolated from unheated milk slowly produced in this medium a definite alkalinity without peptonization. Those recovered from heated milk frequently seemed to cause no change whatsoever. Some, however, showed properties corresponding to those mentioned in the original description, whereas others after several days caused a slight reduction of litmus. At times the organism occurred in great numbers and, like *Str. lact.*, overgrew the spore-bearers after the milk had been incubated for two days.

Micrococcus cremoides and a few unidentified organisms were isolated occasionally. However, they did not appear with any regularity and could not be considered as common bacteria capable of playing a definite part in the reactions of heated milk. No bacteria belonging to the *B. coli.* or *Bact. aërogenes* groups were encountered, nor were any other gas producers ever recovered.

The reactions of milk heated to 65° C. resembled in many ways those observed in the 60° milk. After one day's incubation some tubes were peptonized, others coagulated, still others remained unchanged and, as in the case of the 60° milk, tubes from a single specimen often showed as wide variations as those from different samples. In from two to four days peptonization usually occurred, occasionally with the production of a little gas. At times only a normal clotting was observed. Transfers to dextrose broth in fermentation tubes occasionally caused some production of gas, yet no gas-producing aërobic organisms could be recovered either from the milk or the dextrose broth. Plates made from the milk at the end of the first day's incubation sometimes contained only colonies of the spore-bearing types. At other times *Str. lact.* and *Bact. troilii* also were present. In milk incubated for two days these organisms frequently were found to have overgrown the other varieties, so that their colonies would persist to the exclusion of the spore-bearing type in the plates of greatest dilution. Like the cultures of *Str. lact.* and *Bact. troilii* isolated from 60° milk, these strains usually produced little effect when inoculated into sterile milk; and upon plain agar many failed to grow. No other organisms were ever encountered.

The milk heated to 70, 80 and 85° C. became peptonized in from one to four days. Normal clotting was never observed; instead there was usually a relatively small coagulum containing gas bubbles. When transferred to dextrose broth a definite amount of gas was commonly produced. From this broth and from the heated milk only the ordinary non-gas-producing aërobic spore-bearers could be isolated by the usual process of plating.

As a control to these results, the thermal death-points in milk of the non-spore-bearing bacteria recovered were roughly estimated by the following method: Fresh cultures of the organisms were transferred to sterile milk, and heated in the water-bath to 60, 65 and 70° C. and kept for 15 minutes under conditions identical with those used in the previous experiments. *B. typhosus* was taken as a control. The results were found to be very irregular, when the cotton plugs and the surrounding glass of the milk tubes were not sterilized after inoculation. But when the mouths of the test tubes were thoroughly flamed and the corks burnt after inoculation but before the heat was applied, the results became constant.

Under these circumstances *B. typhosus* was killed at 60° C. The strains of *Str. lact.*, *Bact. troilii*, and *M. cremoides* isolated from milk heated to this temperature survived. At 65° C. *B. typhosus* and *M. cremoides* were killed, but *Str. lact.* and *Bact. troilii* survived. At 70° C. all these organisms were killed. It is worthy of note that all the strains of *Str. lact.* tested did not survive 65°. As mentioned in a previous paper, many strains recovered from unheated milk were found to have a thermal death-point below 60° C.

Of the bacteria isolated from the milk heated to 60 and 65° only the spore-bearers and the various strains of *Str. lact.* and *Bact. troilii* could be considered of frequent occurrence, and the cultural characteristics of these organisms do not completely explain the diverse reactions of the milk in which they are found. This milk either coagulated, usually with the expression of much whey, or else became peptonized after from one to four days' incubation, and in addition also showed gas production under certain conditions. Now *Str. lact.* will coagulate milk, but does so with the production of very little whey, and although the aërobic spore-bearers peptonize milk, they never act very rapidly and, in the writer's experience, do not cause any peptonization during the first few days in the presence of *Str. lacticus*. None of the aërobic organisms isolated produced any gas. Hence the rapid peptonization, marked whey formation, and evolution of gas observed in milk heated to 60 and 65° remain unexplained by what we know of the individual reactions of the organisms isolated.

From milk heated to from 70 to 85° C. only the common spore-bearers were recovered. Such milk peptonizes in from one to four days, usually with the production of a coagulum and the evolution of much gas. Yet the aërobic spore-bearers found therein form no gas in milk and peptonize it slowly, usually without coagulation.

The discrepancy between the reactions of the organisms isolated and the reactions of the milk in which they were found was most marked in the case of the specimens heated to from 70 to 85° C. Despite the fact that such milk commonly showed an evolution of gas after incubation, from it no gas producer could be isolated by aërobic methods. However, Ford [1] and Pryor [2] have recovered the anaërobe, *Bact. welchii*, from milk of this character and have shown that this gaseous reaction probably is due to its influence. They were unable to demonstrate the bacterium in milk heated to 60 and 65° C., but since it was found to exist in milk heated to from 70 to 85°, its presence in specimens heated at lower temperature may be assumed.

This bacterium, in addition to producing gas, has a strong acidifying, coagulating, and whey-producing power in milk when grown anaërobically and for this reason it was thought that the gaseous and other unexplained reactions observed in milk heated to from 60 to 65° might be due to its influence when acting in conjunction with the aërobes surviving the temperatures mentioned. In order to test this theory an attempt was made to reproduce the reactions noted in milk heated at temperatures ranging from 60 to 85° C. by the aid of *Bact. welchii* and the aërobic organisms surviving these temperatures.

With this end in view two strains of *Bact. welchii* were isolated from two samples of 80° milk by a simple method, which is given here in detail, along with another method, as they afford an easy means of recovering *Bact. welchii* in pure culture.

The tops of the closed arms of ordinary fermentation tubes were removed, as in the type designed by Hill, and the resulting apertures tightly corked. One of these tubes was filled with 2 per cent dextrose broth and sterilized in the autoclave at a pressure of 20 pounds. Immediately after cooling it was inoculated with milk which, after being heated to 80° and incubated, showed the presence of gas. Then the fermentation tube was incubated for 24 hours, at the end of which period turbidity appeared throughout the broth and gas was observed in the closed arm. The opening of the bowl was tightly corked and the stopper in the arm carefully removed so as to prevent any mixing of the fluid in the bowl with that in the arm. Then a transfer was made from the arm to the bowl of a similar tube of freshly autoclaved dextrose broth. This preparation was incubated and, after the appearance of turbidity and gas, a similar transfer was made and the process repeated four or five times until the transfers made from the bowl to plain slant agar failed to show any growth when incubated under aërobic conditions. Hanging drops made from such cultures revealed only bacteria indistinguishable morphologically from *Bact. welchii*, and from such preparations it was impossible to isolate any aërobic organism.

When the dextrose broth was not freshly autoclaved, or when daily transfers were made from the bowls instead of from the arms of the fermentation tubes, this phenomenon did not occur. Instead the aërobic spore-bearers continued to grow along with *Bact. welchii* and occasionally even outgrew the latter organism so that no trace of it could be found.

However, it was observed that the fermentation tubes containing mixed cultures of *Bact. welchii* and aërobic and probably anaërobic spore-bearers usually became sterile in from two to five days, and this peculiar reaction led to a second even simpler method of isolating the organism in question. Welch [4] in his original paper has stated that in the tubes of Liborius *Bact. welchii* died in three days, when grown in pure culture and kept aërobically. It was found that in mixed cultures of spore-bearers in dextrose broth in fermentation tubes under these conditions the bacterium died in from three to five days, but that its death was preceded usually by that of the other spore-bearers with which it was mixed. Hence it was often possible to obtain a pure culture of *Bact. welchii* by making a simple transfer on the second, third and fourth days from the bowl containing the mixed culture to freshly autoclaved dextrose broth in fermentation tubes. Sometimes such transfers were sterile, sometimes they contained mixed cultures; in other cases only the aërobes survived. Usually, however, in one of these transfers it was impossible to demonstrate any organism but *Bact. welchii*.

Thus it appears that in freshly autoclaved dextrose broth in the closed arm of the fermentation tube *Bact. welchii* has the power of quickly outgrowing other aërobic and probably anaërobic spore-bearers, and that in the bowl it frequently kills the other spore-bearers before its own death.

As an additional precaution the two cultures obtained by the first method were first plated upon dextrose agar and then replated upon rabbit-blood agar. These two strains were found to correspond very closely with the organism as originally described. They were gram positive, rather large, encapsulated bacteria which caused the typical gaseous reaction in the dead rabbit, and had the power of producing gas in sugar-free agar and broth, as well as from dextrose, lactose and saccharose. They did not grow under aërobic conditions, but produced their reactions in the hydrogen jar, and in the fermentation tube when incubated under atmospheric conditions in freshly autoclaved media containing any one of the sugars considered. They varied somewhat from each other as regards the original description in the time required to produce their action upon milk, and in the amount of whey expressed. In this medium in the fermentation tube both produced an armful of gas and a coagulum riddled with gas bubbles, and caused the expression of so much whey that peptonization was suggested. One strain completed this reaction in 24 hours. The other in this time produced only an armful of gas without any coagulation. However, in 48 hours the two preparations became indistinguishable. Grown in the hydrogen jar in freshly autoclaved milk in test tubes the rapidly acting strain produced in 24 hours the same effect as in the fermentation tube under atmospheric conditions. The other, slowly acting, strain in this time coagulated the milk with the evolution of gas, but with the expression of very little whey.

These two cultures of *Bact. welchii* were now inoculated into milk in combination with each of the organisms previously found capable of surviving the various temperatures considered, in order to observe the influence of the growth of one of the bacteria upon the growth of any one of the remainder.

Str. lacticus, Bact. troilii, B. mesentericus vulgatus, B. cereus and *B. subtilis* were taken as representing the most common species existing in heated milk. Other non-sporulating organisms isolated from milk heated to 60° C. were not considered, since their presence therein is inconstant. The reactions of the two strains of *Bact. welchii* were found not to differ materially when inoculated into milk with the other bacteria employed. Likewise the reactions of the three aërobic spore-bearers, *B. mesentericus vulgatus, B. cereus* and *B. subtilis* resembled each other very closely, when grown in union with *Str. lacticus* or *Bact. welchii*. Hence it was possible, except in one instance, to simplify the experiment by eliminating the slowly acting strain of *Bact. welchii* and by taking *B. subtilis* as representing the aërobic spore-bearing group.

When *Bact. welchii* was transferred along with *Str. lacticus* the resulting reaction was identical with that seen when *Str. lact.* alone was inoculated into milk. But when transferred with either *Bact. troilii* or *B. subtilis* there occurred in from 24 to 48 hours a condition similar to that noticed in milk inoculated with *Bact. welchii* when incubated under anaërobic conditions; the milk was coagulated and rendered violently acid; the coagulum was riddled with gas bubbles, and in addition peptonization or marked whey production was produced.

Bact. troilii grown with *B. subtilis* or *Str. lacticus* produced no visible change from the reactions caused by the latter organisms when transferred singly to milk.

When *B. subtilis* was inoculated into milk with *Str. lacticus* the reaction of the latter organism was hastened, that of the former inhibited. Thus in 24 hours the two bacteria produced in milk a soft coagulum, whereas alone *Str. lact.* did not cause this result until 2 days had elapsed. The peptonization produced by *B. subt.* in 48 hours when grown singly did not appear until the end of a week, and then was too slight to be absolutely definite.

Next the influence of heat upon the bacteria already mentioned was studied by comparing their reactions in milk with those which occurred when the milk was heated after inoculation.

The culture of *Str. lact.* selected possessed a thermal death point between 65 and 70° C. This strain caused acidity without coagulation after 24 hours. In 2 days it produced a solid coagulum with very little or no whey and reduced the litmus. In 3 days more whey was expressed, but no peptonization or gas production was ever caused.

When after inoculation the milk was heated to 60 and 65° for 15 minutes, the time of the reaction was lengthened slightly in the former case, markedly in the latter. Thus, in the milk heated to 60° C. there was produced in 48 hours a soft, instead of the hard, coagulum noted in the unheated specimen. But after heating to 65° only acidity occurred in the same length of time, and coagulation was delayed until 4 days had elapsed, at which period the condition was practically identical with the reaction occurring in 2 days in the unheated control.

The strain of the *Bact. troilii* used had little or no effect upon litmus milk in 48 hours. Later it produced a slight reduction of the litmus. No other reaction was ever noticed. Its thermal death point was found to be between 65 and 70° C., but its action upon the milk was produced too slowly to be affected by the heat applied.

B. subtilis caused no change in milk in 24 hours. After 48 hours it produced a slight peptonization, which became marked in 3 or 4 days. There was no definite coagulation. The reaction was faintly acid. After heating to 60° beginning peptonization was delayed until 3 days had elapsed, and did not become marked until after 4 days.

Bact. welchii failed to grow in milk in test-tubes under aërobic conditions.

An attempt was now made to reproduce the reactions occurring in milk heated to temperatures ranging from 60 to 85° by means of the organisms surviving therein. Milk heated to 60° either coagulates with the expression of varying amounts of whey but without gas production, or else becomes peptonized. Under certain conditions gas is formed. In it *Str. lact., Bact. troilii, B. subt.* and *Bact. welchii* survive. When these organisms were transferred to sterile milk and incubated, the

medium became riddled with gas and reacted very much like that inoculated with *Bact. welchii* alone, when grown anaërobically. This experiment would seem to indicate that *Str. lact.* without the application of heat, is not capable of hindering the reaction of *Bact welchii*, which occurs in the presence of the spore-bearers and *Bact. troilii*, and this in spite of the fact already noted that *Str. lacticus*, unaided by heat, inhibits the effect produced by the aërobic spore-bearers upon milk. Thus it would seem that the coagulation with little or no gas or peptonization observed in raw milk requires the influence of some other organism. In this connection it is worthy of note that when *Bact. aërogenes*, a common inhabitant of unheated milk, was added to the mixture, the milk coagulated in a manner similar to that usually seen in unheated market milk.

When, after inoculation with the four organisms first employed, the milk was heated to 60°, a different result was obtained. Under these conditions the growth of *B. subtilis* is delayed while the action of *Str. lact.* is inhibited very slightly. In consequence the latter organism dominated the reaction and produced in 48 hours a result similar to that seen in 60° milk when it curdles without gas or peptonization.

A second result was obtained when the entire contents of an agar slant culture of *B. subtilis* was transferred to a test-tube of milk and the usual amounts of *Str. lact.*, *Bact. troilii* and *Bact. welchii* were added and the heat was applied. Here *B. subtilis* dominated the reaction and peptonized the medium in 24 hours. In addition a small gaseous coagulum showed that *Bact. welchii* had been enabled to act. In this case the result again was similar to one at times observed in 60° milk, and evidently was due to the overwhelming amount of *B. subtilis* used in the experiment. It suggests that the peptonization at times observed in 60° milk may be due to the presence therein of an excessive amount of aërobic spore-bearers.

Milk heated to 65° reacts in a manner similar to that of 60° milk, but under this condition peptonization with gas production is more common. From it may be isolated the same four organisms. When these bacteria were transferred to sterile milk and the medium was heated to 65°, it became coagulated, peptonized and gaseous in 48 hours, thus reproducing the reaction noted. It is evident that here the heat used so delayed the action of *Str. lact.*, that it was unable to inhibit *B. subtilis*. The latter was thus enabled to grow and in this way cause *Bact. welchii* to develop and produce gas as it does when *B. subtilis* and *Bact. welchii* alone are transferred to milk. In this case a different result was obtained when *B. mesentericus vulgatus* and the slowly acting strain of *Bact. welchii* were substituted for *B. subtilis* and the rapidly acting strain of the latter organism. This combination produced in 24 hours only a slight acidity. In 48 hours it caused coagulation with the expression of much whey, but without evident peptonization and with the evolution of very little gas. This reaction is not unlike that which sometimes occurs in 65° milk.

Milk heated to from 70 to 85° in the writer's experience contains only the aërobic and anaërobic spore-bearers. When *Bact. welchii* and *B. subtilis* were transferred to this medium and it was heated to 80°, coagulation with peptonization and gas production ensued after from 24 to 48 hours' incubation. This is the common condition observed in milk heated at the temperature considered. Thus it is seen to be possible by means of *Bact. welchii*, grown in union with the aërobes existing in heated milk, to simulate many of the reactions of the milk in which they are found.

CONCLUSIONS.

1. In milk heated to 60 and 65° C. for 15 minutes *Streptococcus lacticus*, *Bact. troilii* and the spore-bearers survive. They can be recovered from peptonized as well as from normally clotted milk, but their cultural activities do not completely explain the reactions of the milk in which they are found.

2. Other non-spore-bearing organisms are encountered occasionally in milk heated to 60° C. Their scarcity makes it seem probable that they play an unimportant rôle in the reactions of heated milk. They were not encountered in milk heated to 65° C.

3. No gas-producing aërobes were isolated from milk heated to 60° C.

4. From milk heated to 70 and 85° C. only the aërobic spore-bearers were recovered by the common method of plating. The cultural activities of this group do not explain the reactions seen in milk heated to these temperatures.

5. *Bact. welchii* assumes the power of growth in milk under aërobic conditions when transferred to this medium with the common aërobic spore-bearers or with *Bact. troilii* (Matzuschita). Under these circumstances its reactions overwhelm those of the bacteria with which it grows.

6. When the organisms employed are heated to 60° C. *Streptococcus lacticus* inhibits the action produced upon milk by *Bact. welchii* in the presence of *Bact. troilii* and the aërobic spore-bearers, provided these are not markedly in excess.

7. *Streptococcus lacticus* fails to inhibit this reaction when the aërobic spore-bearers are present in vast numbers, or when no heat is applied.

8. It does so after heating to 65° only in the presence of a slowly acting strain of *Bact. welchii*.

9. The reactions observed in milk heated at temperatures ranging from 60 to 85° C. may be simulated, in the presence of *Bact. welchii*, by the growth of the aërobes commonly surviving the temperatures considered, after the application of the desired degree of heat.

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THE RELATIONS OF SPLANCHNOPTOSIS TO GASTRIC ACIDITY.

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Opinions as to the relationship, if any, that obtains between the acidity of the gastric juice and the various grades of ptosis of the gastro-intestinal viscera, differ very widely. Lockwood, Aaron and Joseph Sailer claim that in ptotic stomachs hyperacidity is found more frequently than subacidity. Steele, Francine and T. R. Brown hold that diminution of free hydrochloric acid is the rule. Still a third group of investigators, including Boas, dismiss the matter with the statement that in cases of ptosis the results of chemical examination are variable, and for reasons not always readily discernible all kinds of deviation from the normal occur.

Lockwood, in a series of 250 cases, found that over four-fifths of the patients showed a normal or hyperacid gastric juice. He gives the following table, but does not state just how the results were computed.

	Per cent.
Achylia was present in	9.5
Subacidity was present in	8.0
Normal acidity was present in	55.6
Hyperacidity was present in	27.4

In a series of gastric analyses as large as the above there will always be found a considerable number of cases that cannot be classified simply as belonging to one of the three groups of normal acidity, hyperacidity, or diminished acidity cases, for the very good reason that many of them fall in more than one group. A patient may belong to the normal acidity class as regards his free hydrochloric acid, and at the same time show hyperacidity for his total acids; and, conversely, his total acidity may fall well within the normal limits (40-60), while his free hydrochloric acid is much below the accepted normal (20-40).

In the writer's series of 200 examinations, 42 such overlapping cases were found. There were 19 cases in which the free hydrochloric acid was normal, with the total acidity well over 60. One patient, with a free hydrochloric of 27, showed a total acidity of 92. A second, with a free hydrochloric of 32, had a total acidity also of 92. These two patients may truly be said to have had a hyperacidity, but not a hyperchlorhydria. In 18 cases the total acidity was found to be normal, with the free hydrochloric either below or above normal. One patient, with a total acidity of 50, showed a free hydrochloric of 5; another, with a total acidity of 48, had a free hydrochloric of 0. Five patients showed a normal free hydrochloric acid co-existent with a total acidity below the normal.

How are such cases that fall in two different groups to be classified? Obviously the only possible way that insures mathematically accurate results is to consider all cases from the view-point (a) of increased or diminished acidity as regards the free hydrochloric acid alone; and (b) of increased or diminished acidity as regards the total acids alone. No other procedure is reasonable, and any analysis not taking this fact into consideration is meaningless. This point, which we consider of much importance, may possibly help to explain the conflicting reports and widely diverging views of many writers regarding the relations of splanchnoptosis and gastric acidity.

Among his conclusions Lockwood says: "The acidity in gastroptosis depends largely upon the degree of the associated atony; the more marked the atony the greater is the tendency toward hyperacidity." Francine, from a study of 70 cases, reports: "There was a slight diminution in free hydrochloric acid with no or slight dilatation, while as the dilatation became more marked the free hydrochloric acid diminished, and was absent in most of the patients in very high grades of dilatation; thus suggesting that the subsequent dilatation is of more importance than the ptosis as regards the gastric secretions." Thus both authorities, while reaching opposite conclusions, agree that in ptotic stomachs the acidity depends largely upon the amount of associated atony.

The present study was undertaken to accurately determine the effect that ptosis of the stomach and bowel have upon the gastric juice, without any consideration of the causal factors underlying this effect. How these secretory changes have been brought about, whether by circulatory interference due to pressure and position, by reflex irritation through drag and pull on the sympathetic plexus, or whether they are the result of atrophy and atony, has not been entered into. Our purpose is to report the findings in a series of 200 thoroughly worked up and verified cases of splanchnoptosis. The cases all occurred in patients who applied for relief, from many and various digestive symptoms, to the gastro-intestinal clinic of The Johns Hopkins Hospital Dispensary, and who in the course of routine examinations were discovered to present well-marked instances of ptosis. The diagnosis was in every case confirmed by fluoroscopic examination, the method being to administer one ounce of bismuth subcarbonate 18 hours previously, and a like amount immediately before the fluoroscopic examination.

The cases have been arbitrarily divided into three groups according to the degree of descensus, and designated as instances of ptosis of the first, second or third degree, respectively. In first-degree cases are included patients in whom the greater curvature of the stomach reached to the level of the pelvic brim; in second-degree cases those in whom the greater curvature was found below the level of the pelvic brim; and in third-degree cases those in whom the stomach reached to the bottom of the pelvis.

The gastric analyses were made after the usual Ewald test-breakfast of one slice of bread and 250 cc. of water; the stomach contents being aspirated 45 minutes after ingestion. The test-breakfast was, as a rule, fairly well digested and showed no constant abnormality. In expressing normal, increased, or

diminished acidities, the usual text-book figures of 20-40 for the free hydrochloric acid and 40-60 for the total acid have, of course, been used.

There were 110 females and 90 males. The high proportion of males is extremely interesting, inasmuch as many authorities still regard splanchnoptosis as an ailment largely peculiar to women, and, according to the statistics of one recent writer, females are more frequent sufferers than males in the proportion of 7 to 1.

The ages varied from 15 to 76 years; over 60 per cent of the patients being between 20 and 40 years of age. No patient under 15 years of age is treated in the clinic.

There are 25 cases of ptosis of the first degree, 140 cases of the second degree, and 35 cases of the third degree. As one would expect, the most frequent accompaniments of the ptosis were adhesions and atony. Marked adhesions were present in 40 cases and marked atony in 50 cases.

It is of interest to note that the average amount of stomach contents recovered by aspiration after the test meal increases with the degree of descent of this organ.

In ptosis of the first degree the average amount recovered was ..... 41 cc.
In ptosis of the second degree the average amount recovered was ..... 56 cc.
In ptosis of the third degree the average amount recovered was ..... 72 cc.

First Degree Ptosis.—In this group, comprising mild cases in which the greater curvature reached no lower than the level of the pelvic brim, were found 25 cases—14 in females and 11 in males. The gastric analysis gave the following results:

FREE HYDROCHLORIC ACID.

	Per cent.
Normal acidity was present in	40
Hyperacidity was present in	28
Subacidity was present in	20
Achylia was present in	12
Subacidity or achylia was present in	32

TOTAL ACIDITY.

	Per cent.
Normal acidity was present in	32
Hyperacidity was present in	48
Subacidity was present in	20

Second Degree Ptosis.—In this group of moderate ptosis, comprising those cases in which the greater curvature reached below the level of the pelvic brim, were found 140 cases—73 in females and 67 in males.

FREE HYDROCHLORIC ACID.

	Per cent.
Normal acidity was present in	49.2
Hyperacidity was present in	12.8
Subacidity was present in	24.2
Achylia was present in	13.5
Subacidity or achylia was present in	37.7

TOTAL ACIDITY.

	Per cent.
Normal acidity was present in	46.4
Hyperacidity was present in	18.5
Subacidity was present in	35.1

Third Degree Ptosis.—This group, including those high-grade ptoses in which the stomach was found at the bottom of the pelvis, contained 35 patients—23 females and 12 males.

FREE HYDROCHLORIC ACID.

	Per cent.
Normal acidity was present in	48.5
Hyperacidity was present in	25.7
Subacidity was present in	17.1
Achylia was present in	8.5
Subacidity or achylia was present in	25.6

TOTAL ACIDITY.

	Per cent.
Normal acidity was present in	40
Hyperacidity was present in	34.2
Subacidity was present in	25.7

From these tables it would appear that no definite relationship can be established between the degree of ptosis and that of diminished acidity, the cases of the second group showing a much lower acidity percentage than those of either the first or third. An average of these three tables gives the following percentages for the 200 cases of ptosis of all three grades.

FREE HYDROCHLORIC ACID.

	Per cent.
Normal acidity was present in	48
Hyperacidity was present in	17
Subacidity was present in	22.5
Achylia was present in	12.5
Subacidity or achylia was present in	35

TOTAL ACIDITY.

	Per cent.
Normal acidity was present in	43.5
Hyperacidity was present in	25
Subacidity was present in	31.5

CONCLUSION.

1. The free hydrochloric acid was found to be normal or diminished in 83 per cent of all cases. The total acidity was normal or diminished in 75 per cent of all cases. Therefore, it would seem quite conclusive from these figures that in *ptotic stomachs there is a general tendency toward diminished acidity; and that hypochlorhydria and achylia are more frequently met with than hyperchlorhydria, the ratio being about 2 to 1.*

2. It is of interest to note that the 50 cases complicated by marked atony gave a still higher percentage of diminished acidity than the cases in which atony was not so marked, as is shown in the following table:

FIFTY CASES OF SPLANCHNOPTOSIS OF ALL DEGREES WITH MARKED ATONY.

FREE HYDROCHLORIC ACID.

	Per cent.
Normal acidity was present in	42
Hyperacidity was present in	18
Subacidity or achylia was present in	40

TOTAL ACIDITY.

	Per cent.
Normal acidity was present in	36
Hyperacidity was present in	30
Subacidity was present in	34

Apparently the acidity in gastroptosis is largely influenced by the amount of associated atony—the greater the atony, the lower the acidity.

3. *Achylia was present in 12.5 per cent of all cases.* This at first sight seems to be a rather high figure. Lockwood, however, reports that in his experience achylia was present in nearly 7 per cent of all patients applying for relief from gastro-intestinal disorders. The difference between these figures is hardly great enough to suggest a causal relationship between the two conditions.

To Dr. Thomas R. Brown, at whose suggestion this report is made, I wish to express my most sincere thanks for the privilege of studying these cases.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

APRIL 19, 1915.

1. **The Blood and the Blood Vessels in Hemophilia and other Hemorrhagic Diseases.** (Abstract.) DR. ALFRED T. HESS, New York City.

It is impossible at the present time to classify the hemorrhagic diseases. However, two main groups may be distinguished: hemophilia and purpura. By hemophilia is meant the type of disease which is characterized by its hereditary nature and by the fact that it is transmitted almost always to the male, the female showing no manifestations of the disease. Clinically, its main criterion is the great delay in the coagulation of the blood. The purpuras, on the other hand, show an almost normal coagulation time of the blood, and occur in females as frequently as in males. This group is characterized by a diminished number of the blood platelets, which are normal in hemophilia; by an increase in the bleeding time; by the occurrence of hemorrhage at the site of subcutaneous puncture; by the appearance of many small petechial spots, and by the freedom of the joints from hemorrhagic involvement. In addition to these signs, we have described what may be termed *the capillary resistance test*, which is chiefly present in the purpuric conditions and has been found to be absent in hemophilia. By this is meant the phenomenon of the appearance of petechial spots on the fore arm following the application of a tourniquet for a definite period to the upper arm, in other words, after subjection of the vessel walls to this increase of pressure.

However, these two groups of hemophilia and purpura overlap to a certain extent. We have met with an instance where true hemophilia existed in the male, and purpura, manifesting the various symptoms just enumerated, was present in the female. Furthermore, purpura not infrequently occurs as a family disease, so that a hereditary history does not indicate the existence of hemophilia. There are other borderline cases.

Melena neonatorum is one of the most important groups under purpura. From a pathogenetic point of view, this must not be considered an entity. It includes the toxic, hemophilic and purpuric type.

The defect leading to hemophilia is not definitely known. It has been generally determined that there is no deficiency of calcium. In one case followed for a considerable period, a definite deficiency of calcium was established. This was determined by means of the calcium estimations of the blood, by the hastening of coagulation following the addition of minimal amounts of calcium to the blood (a procedure which delays or does not hasten the coagulation of normal blood), and by metabolism studies which show that in this case there was a negative balance of calcium, whereas in a typical case of hemophilia, the calcium balance was positive. This case, a boy of about 4 years, was judged to have hemophilia, as the coagulation of his blood was delayed and the platelet count was always normal.

The blood vessels vary in their resistance greatly among normal children. They were found to be somewhat weak among children having tuberculosis. In a study of numerous cases of infantile scurvy, we were led to conclude that the blood was but slightly influenced by this disorder, but that the hemorrhages, so characteristic of this disease, were due to involvement of the blood vessels.

From a clinical standpoint it would seem that too much stress is at present being laid upon the coagulation time of the blood and even from blood obtained not directly from the blood vessels. Operations are undertaken if the clotting time is reported as normal. This leads to serious or fatal consequences. It is far more important from this point of view to ascertain the number of platelets, the bleeding time, and the appearance or absence of hemorrhage following subcutaneous puncture.

2. **Experimental Removal of the Pineal Body.** DR. W. E. DANDY.

A satisfactory method of approach to the pineal, with removal, was demonstrated, with drawings by Mr. Broedel of the different steps in the operation. The operation as evolved has been the result of three years of unsuccessful attempts, the animals invariably dying from intraventricular hemorrhage. This was due to the necessity of opening the ventricles and a bleeding which occurred synchronously.

The first attempts to remove the pineal, and which were finally successful, were by an approach under the corpus callosum and under the great vein of Galen, following the interquadrigeminal group to the pineal. It was finally decided that the difficulties of approach, the time which it consumed and the capricious results necessitated a new method. This new method is very simple and can be done in from one-half to one hour on very young puppies. In this method the corpus callosum is split posteriorly for a short distance and the roof of the third ventricle perforated, releasing the fluid, when the pineal is beautifully exposed under the great vein of Galen at its origin upon the two small veins of Galen. By this method about 30 animals between the ages of 10 days and one year were pinealectomized, and all with perfectly negative result. There was absolutely no evidence of any precocity, either sexual, somatic or mental. This is the first successful operative procedure for the removal of the pineal body.

APRIL 26, 1915.

THE ETIOLOGY OF TYPHUS EXANTHEMATICUS.

(Abstracts.)*

1. **Bacteriological Studies.** DR. HARRY PLOTZ, New York City.

In a preliminary communication published in the *Journal of the American Medical Association*, of May 16, 1914, I described an organism which I considered to be the etiological agent in typhus exanthematicus. Since that time I have had the opportunity of studying a much larger series of cases, and the results together with the serological and experimental studies have confirmed the opinion then expressed. The differentiation of the mild endemic form of typhus fever seen in New York from other

* Complete reports will be published shortly in the *Journal of Infectious Diseases*.

fevers is due to the clinical insight of Dr. Nathan E. Brill. The similarity of typhus fever had been noted clinically, and the striking cross immunity experiments of Anderson and Goldberger demonstrated that the condition was most likely a mild form of typhus fever. As our studies give the definite proof that these cases are instances of typhus fever, we shall designate the European cases, epidemic typhus fever, and the New York cases, endemic typhus fever.

It had been demonstrated by early experiments that the virus exists in the circulating blood during the febrile period of the disease and that the virus is not filtrable. Ricketts and Wilder pointed out that the disease need not necessarily be caused by a protozoon, although it be insect-borne. Aerobic cultures made by different observers and by myself proved negative.

Up to the present time we have studied 11 cases of European epidemic typhus fever and 40 cases of the local endemic form of the disease. The former were studied through the kindness of Dr. Joseph J. O'Connell, health officer of the port of New York, and the latter through the courtesy of the attending physicians of Mount Sinai Hospital. The work was carried out under the direction and with the helpful assistance of Dr. E. Libman. We are indebted to Dr. F. S. Mandlebaum, pathologist of the hospital, for many courtesies and for the facilities of the laboratory.

Aerobic studies, made according to the method of Rabinowitch, all proved negative. Anaerobic studies were carried out according to the method introduced by Veillon, modified in that serum glucose agar originally suggested as an optimum medium by Libman, was used instead of glucose agar. All ascitic fluids used were thoroughly studied aerobically and anaerobically, the presence of hemoglobinophilic organisms being excluded by their use.

Colonies of the organism usually appear in from three to 16 days. After they have developed they are inoculated on slants of ½ per cent serum glucose agar, the tubes then being inserted into Buchner tubes. The colonies usually appear in the lower two or three centimeters of the tube. There is first a small opaque spot which grows larger and is surrounded by a brownish area of precipitation. On cross-section the colony is Y-shaped, brownish in appearance and soft in consistency. The arms of the Y are fusiform.

The organism is a small pleomorphic Gram-positive bacillus, which is non-motile, non-encapsulated and not acid fast. Most of the organisms are straight, occasional ones are rounded or slightly pointed; coccoid forms also occur. Degeneration and involution forms appear early. Spores are not present. Polar bodies are occasionally demonstrable.

Besides the studies made in Buchner tubes, inoculations were made into a variety of media in the long tubes of the type used by Noguchi. There is no growth on agar or sugar-free bouillon after 20 days observation. Growth is present in ½ per cent glucose agar with ascitic fluid and kidney tissue, but is better in 2 per cent glucose agar. There is a minute flocculent growth at the bottom of the glucose bouillon tube after eight days.

In Buchner tubes, after three days on glucose serum agar, there is a creamy white growth which later may become light brown in color. There is moderate precipitation which increases on subculture. The growth on other media is described in the full publication.

The organism from the epidemic and endemic cases was found to produce acid and precipitation in glucose, maltose, galactose and inulin and not in raffinose, mannite, arabinose, saccharose, dextrine and lactose. The organism is an obligatory anaerobe.

The organism was recovered from the blood in seven cases of epidemic typhus fever during the febrile stage; it was recovered from an eighth case by culture of the blood from an infected guinea-pig.

Of 34 endemic cases, 53 per cent yielded the bacillus. In two endemic cases the organism was found in one, 12 hours, and in the other, 36 hours after the crisis. 198 control cases did not yield the organism. The organism occurs more frequently early in the the disease. It occurs in larger numbers in the epidemic cases than in the endemic cases.

Considered in conjunction with the serological and experimental evidence which follows, these facts prove that this bacillus is the etiological factor in typhus exanthematicus. Following a very kind suggestion of Professor William H. Welch, the organism has been named bacillus typhi exanthematici.

2. Serological Studies. DR. PETER K. OLITSKY, New York City.

With the use of an antigen made up of strains of the typhus bacillus from endemic and epidemic cases, 11 cases of epidemic and 34 cases of endemic typhus fever were studied. Of 25 cases studied at the height of the disease, only two were positive. Of 10 cases studied at the crisis, four were positive. In the post-critical stage of the disease, nine epidemic and 30 endemic cases were investigated, and 71.8 per cent were found to give positive reactions. The maximum concentration was found to occur between the second and twelfth day after the crisis. Observations were made as regards duration of the antibodies. 104 control cases showed complete absence of complement binding bodies. Complement fixation studies made with the serum of typhus fever cases and antigens made from various organisms other than the typhus bacillus gave negative results.

Positive agglutinations were obtained in more instances than positive complement fixation tests. Only reactions in dilutions of 1-50 or higher were considered positive. Of 24 cases tested before the crisis, all were negative, except two which were tested one day before the crisis, both of which had a titre of 1 to 100. Of 10 cases tested on the day of crisis, three were positive and seven were negative. After the crisis, 38 cases were studied, 92.6 per cent of which were positive. Agglutinins have been demonstrated as late as five months after the crisis. Of a very large series of control cases no case had a reaction in a dilution of over 1 to 50 except three cases in which the occurrence of a previous attack of typhus fever could not be excluded. In these cases the reactions varied from 1 to 100 to 1 to 200. Control studies made by testing the serum of typhus cases against various organisms other than the typhus bacillus proved negative.

Investigations made concerning precipitation reactions showed that the curve was the same as that with the other antibodies, the most frequent results being obtained after the crisis. Serum from cases other than typhus fever gave negative results.

The opsonic index increases at the crisis and remains high in the convalescent stage of the disease. Similar rises were noted in artificially immunized serum (rabbit's). Phagocytosis is probably an important factor in overcoming the infection.

Cross-fixation investigations and cross-agglutination tests demonstrated that the organism obtained from epidemic typhus fever and the one from endemic typhus fever are two strains of the same bacterium.

A study of the serum of monkeys that had reacted to the typhus virus, showed that complement fixation and agglutination tests were usually positive after the crisis. The serum of immune guinea-pigs contained neither agglutinin nor complement fixing bodies. It is most probable that this animal develops its high grade of immunity by means of its tissue elements and only to a very slight degree by means of the circulating blood. Rabbits are not susceptible to the typhus bacillus in small amounts. When small yet increasing amounts of bacteria are given, they develop very potent immune serum.

The observations which I have described allow of only one conclusion—typhus fever is a reaction against the organism which has been isolated by Dr. Plotz.

3. Experimental Studies. DRS. GEORGE BAEHR, HARRY PLOTZ and PETER K. OLITSKY, New York City.

For the purpose of ascertaining whether the organism recovered from the blood of typhus fever patients was also found in animals having experimental typhus fever, a series of 24 guinea-pigs was

inoculated with defibrinated blood obtained from patients or animals with the disease. Blood for cultures was obtained by direct aspiration of the heart. From one-third of these guinea-pigs the same bacillus was isolated that had been obtained from the blood of individuals with typhus fever. The number of colonies found averaged about one per cubic centimeter of blood. The organisms were found most frequently in animals having severe reactions. The majority of the blood cultures were positive when taken between 24 and 72 hours after the onset of the fever. This is the time at which the fever is highest.

By inoculation of two strains of bacilli obtained from epidemic typhus cases, a typical reaction was produced in two guinea-pigs. The blood of one of these guinea-pigs was cultured on the third day of the reaction and the organism recovered. Other guinea-pigs or monkeys were later inoculated with these two strains of bacilli or with strains from other epidemic cases which had been in artificial media for more than three or four weeks, and all strains were found to have completely lost their virulence. In each instance the inoculation was followed only by a slight transitory rise in temperature during the first 36 hours, a reaction also observed in the experiments with virulent organisms and apparently due to a toxin reaction. After cultivation on artificial media for more than a month all strains of epidemic organisms lost this toxin action. The bacilli from endemic cases were found to lose their virulence outside the body still more rapidly than those from epidemic cases. These organisms were not only avirulent, but did not even possess the power of producing a toxic rise in temperature after inoculation, a property only lost by the epidemic typhus organisms after cultivation for over a month. The variation in virulence and in toxin production of the epidemic and endemic strains is the only essential difference which we have been able to demonstrate.

It was found that typhus blood which contains no bacilli or only very few bacilli is not infective for animals. It appears from a series of 57 experiments that infectivity is absolutely dependent upon the presence of a sufficient number of these bacilli. This in itself is conclusive evidence of their etiological significance.

Recently a study has been begun upon individuals who have merely been exposed to the infection of typhus fever. The interesting observation has been made that after the exposure some of these typhus contacts may react with the production of specific immune bodies without having had any clinical evidences of the disease.

DISCUSSION.

Dr. Anderson: Mr. President: I consider it a very great privilege to have been present to-night and heard the three papers that have just been presented. As perhaps some of you may know, the question of typhus fever has been one in which I have been considerably interested for the past three or four years and I have had the privilege of contributing something to our later knowledge of typhus fever.

In this work but slight attention was given to attempts to cultivate the organism and our cultural methods were confined almost entirely to the use of the ordinary aerobic and anaerobic methods in order to demonstrate that the blood used in our experiments was free from extraneous organisms.

There is nothing that I can add to what the others have said, other than to say that the evidence presented here this evening appears to me to be almost convincing and I shall be surprised if the work here presented will not be confirmed very speedily by others.

I was especially interested in the statements as to the amount of blood necessary to be used in order to obtain a growth and note that the minimum amount of blood in which growth was usually obtained corresponds closely with the amount that we have employed to be surely infective for guinea-pigs.

With your permission, Mr. President, I should like to say just a few words in regard to the prevention of typhus fever.

I do not know of any experimental evidence to the effect that typhus fever is transmitted in any other way than by the bite of the body louse and possibly by the bite of the head louse. The fact that the disease may be caused by a bacterium does not necessarily preclude the possibility of transmission by other biting insects, but our experiments, as well as those of others, with fleas and bedbugs have all been negative. If, then, the louse is the chief means, or the only means, by which the disease is transmitted we are able, from this fact, to deduce certain fundamental factors in regard to the prevention of typhus fever and these may be broadly grouped under three headings:

First, the reduction of lice infestation among the population in general. This is, to a large extent, a question of education, except in institutions such as bath houses, lodging houses, and similar places where numbers of persons may congregate and over which the sanitary authorities may exercise control.

Second, the destruction of lice on the persons, and in the surroundings, of those suffering from typhus fever, of typhus fever suspects and contacts. This is a simpler procedure than the first one because, according to our experiments, the louse requires frequent feedings of blood in order to maintain life and therefore our attention under this procedure may be mainly directed to the destruction of lice on the patient and in the surroundings recently occupied by persons suffering from the disease.

The third measure is to prevent or minimize the chances of persons in contact with cases of typhus fever being bitten by lice. This applies especially to physicians and nurses in attendance upon cases of the disease.

An important practical point to bear in mind is that the "striking distance" of the louse, and therefore of typhus fever, is very much less than that of the flea, which transmits bubonic plague, and of the mosquito, which transmits malaria and yellow fever. Therefore, we may confine our attention, for practical purposes, to surroundings recently occupied by persons suffering from typhus.

I should like to suggest a fourth measure, which I believe would be advisable for those proposing to visit localities in which typhus fever is prevailing in epidemic form attended with high mortality. This measure is the inoculation with the so-called Brill's disease or mild typhus fever in order that an attack of the mild form of the disease may be induced in the individual, recovery from which would afford immunity against the virulent type. The case mortality in the United States from the mild form of typhus fever is certainly not over one in a hundred and perhaps less, while the case mortality in Serbia may be 20 per cent or possibly more.

I thank you very much.

Dr. Libman: I should like to say a few words for Dr. Brill who was anxious to come down here to-night, but was prevented from doing so by other engagements. He believes that the work that has been presented here to-night gives the definite proof that the cases which he described are cases of typhus fever. He was inclined to believe this when Drs. Anderson and Goldberger published their studies, but would not accept their work as final proof because he thought there might be a relationship between the two diseases such as exists between paratyphoid and typhoid fever. One other point is that while he believes it may very well be that typhus fever is transmitted only by the louse, there are several points that need elucidation as, for instance, the fact that the cases which he has seen in New York occurred quite as frequently in the warm as in the cold part of the year. Apart from this, the New York cases are almost never seen attacking a family.

It has been most interesting for us to watch this work. It was a very good example of what can be accomplished by a simple line of reasoning. Dr. Plotz saw a few cases of Brill's disease,

while he was a student, and thought he would like to find out the cause. Because the cases described by Dr. Brill were suspected of being instances of mild typhus fever he decided to use the methods which should be employed in trying to discover the etiological agent in typhus fever. He concluded to look for an anaerobic bacterium and found the organism in the first case which he cultured.

It is also interesting for us to realize the importance of previous investigations in this connection and to consider how many results have been obtained by American investigators.

Dr. Anderson has spoken of the possibility of having people who are to be exposed to European typhus fever inoculated with the virus from the Brill's type of cases and go through the disease. However, while it is true that the mortality in the endemic cases is trifling, patients suffering from the disease are often painfully sick. It might be wise if vaccines made from the organisms which are now on hand are not effective, to try the use of vaccines made from virulent organisms obtained from epidemic cases. Dr. Baehr's studies on contacts suggest that there might be a field for the use of vaccination with small numbers of living bacilli.

DR. WELCH: I was extremely interested a year ago when Dr. Plotz was kind enough to show me the results which he had obtained. Even then they were very promising. I do feel that these young investigators are to be most heartily congratulated. Their work is a model of thorough-going scientific accuracy. It is hard to see any point which they have not covered in the space of time at their disposal and with material necessarily limited in amount.

Dr. Libman spoke of the number of American investigators who have contributed. There is one name I should like to mention, whose memory should always be held in great gratitude, and that is young Dr. Ricketts, who died in Mexico as the result of typhus from exposure while working there. He had at the time just accepted the chair of pathology at the University of Pennsylvania. He was one of the most charming and brilliant investigators in the profession.

There are one or two points I would like to comment on. It is most interesting that this appears to be a true bacterium. I would like to inquire whether these investigators consider that there is anywhere a local or more than one local focus of the disease, and that the bacteria which are present in such relatively small numbers are swept into the blood perhaps, and that possibly this is the kind of bacterium which is well known to be associated with various other localized infections. That could hardly be worked out except on the basis of adequate post-mortem examinations. I do not know exactly where one would expect that local focus to be. Conceivably perhaps in the bone marrow. Some years ago we had a few cases of typhus fever brought here from Sparrows Point, and I remember that in examining the bone marrow in those cases, I was struck with some rather remarkable lesions. Is this anything more than a bacteriæmia, or is there a local infection somewhere? If a real bacteriæmia, it is perhaps the only true bacterial bacteriæmia in human pathology. I do not know of another example.

I was thinking all along of the points Dr. Baehr discussed at the end—of how to reconcile these results of the transmissibility of the disease by lice, when such a large amount of blood was needed to convey the disease. Dr. Baehr has probably said all that can be said at present on that point. He has also intimated that it may be that the louse seems to be the sole transmitter of the disease by virtue of the fact that it is a particularly favorable host for the multiplication of the organisms.

I was not quite clear as to one point, but I have no doubt I overlooked it, namely: After the animal has been infected with the culture of the organism—I quite understand that it is difficult and that the organism loses rapidly in virulence, so the number of successful infections must be very few—and after an animal has passed through an infection due to the bacterial invasion, is it then immune from inoculation with the typhus blood? That would strengthen immensely the evidence and would be very significant.

DR. FORD: I think it is interesting to point out that in this disease some of the most important investigations have been carried out by American physicians. Thus, in 1839, Gerhard of Philadelphia first clearly pointed out the distinguishing features of typhoid and typhus, while the earlier papers of Jackson of Boston are also equally important.

I have here a copy of Gregory's book on fevers which I thought might be interesting to show because of the excellent descriptions given. It is interesting to note that Gregory himself expresses an opinion which we have heard expressed here this evening, namely: That of all fevers typhus fever is the most apt to be mistaken for other diseases.

In considering the historical development of our knowledge of typhus fever, how striking it is that so much of our modern knowledge of this disease has come from American investigators.

There are possibly five important points:

First, the differentiation of this disease from typhoid fever.

Second, definite determination that the disease can be transmitted to animals.

Third, mode of transmission through the louse.

Fourth, that we have in this country, both in Mexico and the United States, an endemic disease identical with the typhus fever of the Old World.

Finally, that the disease is bacterial in origin and that a positive agent can be obtained from the blood and identified.

With the exception of the work of Nicolle and his collaborators these advances in our knowledge of typhus fever are all due to the investigations of American scientists, a matter for which we have reason to feel justly proud.

DR. JANEWAY: There are one or two things I want to say to those of you who are occupying most of the benches here to-night. The first one is that this is a beautiful demonstration of the fact that no age is exempt from the possibility of great discoveries. Pasteur did his best work after a hemiplegic attack when along in middle life. Other investigators, as those who have come here to-night, have done remarkable things at the inception of their medical careers. This ought to be a constant stimulus to those of you who are about to enter on your hospital work—to know that a man in the first year of his interneship in a hospital, has been able to put the finishing touches to the problem of the etiology of typhus fever, which has occupied many investigators for nearly a century.

Secondly, Dr. Libman is quite right in his statement that it is not his work. Nevertheless the work could not have been possible except in an environment in which the scientific pabulum for the production of ideas and the refining of methods were not already at hand. For that environment Dr. Libman is responsible. For years he has been founding in New York City what one might call a school of bacteriological study, particularly in blood culture work. There has been no place in the United States where more careful blood culture studies have been made than in the Mt. Sinai Hospital.

In the third place, it is rather wise for us to remember here that the intellectual and scientific atmosphere necessary for this kind of work is not found only in a university. Here is a beautiful piece of work from a hospital with no definite university association. I think that emphasizes perhaps what has been one of the vital points of the Johns Hopkins Medical School all these years—that a medical school without a hospital is even more apt to be sterile than a hospital without a medical school.

DR. BAEHR: Dr. Welch has asked as to the possible existence of some local focus from which the bacteria may be distributed

into the blood. We have searched for such a local focus in animals which have been killed during the course of the disease and have failed to find it in any of the viscera. It will prove interesting to follow Dr. Welch's suggestion and examine the bone marrow with this in view. In reply to Dr. Welch's second question, we can only cite the statements made in our paper that after a reaction produced with the bacilli we have not as yet had an animal live long enough to test its immunity.

The point brought out by Dr. Brill is also very interesting—that the families of individuals with endemic typhus fever very rarely develop the disease. This fact has been considered by some as militating against the identity of Brill's disease and epidemic typhus fever. As many as four cases in one family have been reported in the literature, but this is very unusual.

The explanation may lie in the development of an immunity in the exposed members of a family, similar to that of Dr. B. and Miss L. The family of an endemic patient is exposed to the bites of the lice before their full infectivity has developed. Like Dr. B. and Miss L., they may therefore merely react with the production of antibodies without having had any febrile manifestations of the disease. Later, after the lice have reached the stage of full infectivity, these more or less immune relatives as well as the convalescent patient may act as carriers for their distribution to others.

NOTES ON NEW BOOKS.

Osler's Modern Medicine. Second edition. Vol. III. Diseases of the Digestive System; Diseases of the Urinary System. (*Philadelphia: Lea & Febiger, 1914.*)

Following the policy adopted in the preceding volumes of the second edition we note the general condensation of the chapters by the elimination to a large extent of historical matter and citations from the literature. The work has been well done and the various chapters have been improved and brought up to date, although the absence of the literature deprives it to some degree of its air of authority. The letter press, paper and illustrations are much better than in the first edition.

Among the chapters in the digestive tract, the most notable are: Diseases of the Liver, Gall-bladder and Ducts, by A. O. J. Kelly, revised by Wm. Pepper; The Pancreas, by Opie; The Peritoneum, by Rolleston. In the urological section: Nephritis is covered by J. B. Herrick; Infections of the Kidney, by T. R. Brown; Lithiasis, Tumors, the Prostate, and Genito-urinary diagnosis, by H. H. Young. Altogether the volume is a distinct improvement on the first edition and, with the exceptions noted above, covers the subjects exceedingly well.

Selected Addresses Relating to Education, Biography, Travel, etc. By JAMES TYSON, M. D., LL. D., Professor of Medicine Emeritus, University of Pennsylvania. Cloth, $1.75 net. (*Philadelphia: P. Blakiston's Son & Co., 1914.*)

The reader, at the outset, is most pleasantly impressed by the author's graceful and altogether unusual confession of his threefold reasons for publishing these addresses. Would that all authors were as frank!

The addresses are all characterized by a directness, ease and felicity of expression which gives an added charm. They cover a wide range of educational, biographical and professional topics and, although not of equal merit, are all interesting. They display a deeper religious and spiritual tone than is generally to be found in the deliverances of physicians, who as a rule are little inclined to dwell upon the duty of joyousness, hopefulness, sympathy, faith or charity, or to recommend them to their auditors. The papers on "Hospital Organization," "The Trained Nurse," and the several phases of medical education are full of wisdom derived from large experience interpreted by an open mind.

The memoirs of Smith, Pepper and Gerhard show the heart of the writer and his keen insight into the personal characteristics of his intimate friends and professional associates. They are also worthy tributes to three men who contributed materially to the growth and development of medical science in Philadelphia.

The descriptions of Karlsbad, Vichy and the Engadine furnish a valuable analysis of the merits and demerits of these health resorts, as well as charming descriptions of the scenery and surroundings. His "repeated message," as he happily terms it, will be appreciated by all who read it.

Osler's Modern Medicine. Second edition. Vol. IV. Diseases of the Circulatory System; Diseases of the Blood; Diseases of the Lymphatic System; Diseases of the Ductless Glands; Vaso-motor and Trophic Disorders. (*Philadelphia: Lea & Febiger, 1915.*)

This volume is, in the reviewer's opinion, the best of the system so far issued. In diseases of the circulatory system the principal chapters are contributed by Hoover, Lewis, Babcock, Osler and Alexander Gibson. The section on congenital diseases of the heart, by Maude Abbott, is excellent. Nothing could be finer than Osler's discussion of aneurysm and those who remember his ward classes can renew their enthusiasm in reading this chapter. It would be hard to get together a better group of writers to cover all phases of cardio-vascular pathology.

Section II, on The Blood, is covered by Cabot, and The Hemorrhagic Diatheses, by Pratt, both parts being considerably changed and brought up to date.

In Section III, The Lymphatic System is by Warthin whose extensive pathological experience is very much in evidence; Longcope gives a fine presentation of Hodgkin's Disease.

Section IV, The Ductless Glands, is largely covered by Dock, who gives a good presentation of the modern theories without laying too much stress on any one. The last section, on Vaso-motor and Trophic Disorders, is entirely by Osler and in his best vein.

Were it possible for any system to hold this level of achievement throughout, the publisher and the reader would be mutually fortunate.

Acute General Miliary Tuberculosis. By G. CORNET, M. D., Berlin. Translated by F. S. TINKER, B. A., M. B., B. C., etc. Cloth, $1.50. (*New York: Paul B. Hoeber, 1914.*)

The present volume gives an erudite review of the older literature upon this subject. The pathology and clinical manifestations of the disease are satisfactorily considered and the mechanical features, whereby the circulation is flooded with tubercle bacilli, are rehearsed in detail. The fact, however, that none of the important experimental work upon immunity in tuberculosis, which surely has an important bearing upon the subject, is so much as mentioned, gives the book a somewhat antiquated flavor and it seems a pity that the author has not brought it up abreast with the latest scientific thought. The translation is poor. L. H.

Manual of Bacteriology. By R. TANNER HEWLETT, M. D., F. R. C. P., D. P. H. Fifth edition. Cloth, $4.50. (*St. Louis: C. V. Mosby & Co., 1915.*)

In this volume of 700 pages the author attempts to present and combine the subject matter in such a way that it may be not merely interesting from the standpoint of general bacteriology, but of special value in relation to clinical medicine and to hygiene or public health. In this respect it may be said to serve various

purposes. As a text-book, although somewhat elementary, it is thorough, complete and especially suited to beginners in bacteriology. Also to busy practitioners who desire to keep in close touch with this rapidly progressing science, it will serve a similar purpose. It is also useful as a reference book in that it summarizes the findings of others and gives the original literature. The conclusions reached in regard to some of the still undecided questions in bacteriology are worthy of careful study, because of the ripe experience of the author. The book may also serve as a laboratory manual in general or clinical bacteriology and in hygiene and sanitary investigations. The methods advocated for the bacteriological examination of water, air, soil, sewage, milk and foods are those made use of by standard public health laboratories.

In a brief survey of its contents we find a great deal of merit. The technique described for certain phases of bacteriological work is slightly different from that generally employed but of decided excellence. The descriptions of the methods employed in clinical laboratory diagnosis are brief, but afford all that is essential for beginners. Brief references are made to serum diagnosis, to vaccines and to the methods of their preparation. By including several chapters on higher schizomycetes, the pathogenic protozoa and on diseases, the causative agents of which are generally considered as filtrable viruses, the author adds completeness to his work. To the hygienist the entire volume is significant from the view-point of general bacteriology, but the chapters dealing with the bacteriology of water, air, soil, sewage, milk, foods and disinfection are of special importance. W. W. F.

The Commoner Diseases, their Causes and Effects. By DR. LEONHARD JORES. Authorized translation by WILLIAM A. WOGLOM, M. D. Cloth, $4.00. (*Philadelphia: J. B. Lippincott Company, 1915.*)

This is an excellent book, worthy of the widest popularity. The method of presentation will appeal to students and more particularly to internists, since it gives a pathological picture of disease that corresponds with the clinical picture observed during life. Instead of following the usual custom of describing the various lesions which may affect each organ, the author selects a disease and describes the changes commonly found in a body that has suffered from it. Thus widely scattered lesions are brought together under each caption, and their relation to one another is pointed out. The pathological descriptions are agreeably brief and yet give satisfactory impressions of the lesions. The discussions throughout are cogent and present the important recent developments of medical science. The author gives a broad, clear and interesting view of the relation of clinical medicine to pathology. The translation has been well done. The book has exceptional merit. L. H.

The Heart in Early Life. By G. A. SUTHERLAND, M. D., F. R. C. S. Cloth, $2.00. (*London: Oxford Medical Publications, 1914.*)

This publication is a readable little book of two hundred pages. It is nicely arranged and well printed. The subject matter is divided into three sections: Functional Cardiac Disturbances; Borderland Between Functional and Organic Disease; Organic Heart Disease. The various chapters in these sections deal with the physiology, diagnosis and treatment of the several conditions.

The author makes no effort towards the development of a text-book, but deals rather broadly with the clinical findings, normal and pathological, of the heart in childhood. He points out that the pathological physiology of the child's heart is definitely different from that of the adult and that, therefore, the symptoms and signs are distinctive. He emphasizes normal peculiarities of the youthful heart—the relatively large size, the instability of the vasomotor tone with the possible functional dilatation of the vessels or of the heart itself.

The book is well worth while, in that it points out a fact that is generally not fully comprehended—that in early life functional conditions far outnumber the organic diseases in cases of suspected "heart trouble," and that many of the symptoms, which are truly cardiac in adult life, in childhood are referable to other organs, especially to the nervous system. A diagnosis to be of avail cannot depend on the anamnesis or on the presence of an apical murmur. There must be a complete physical examination with a balancing of all the findings with the functional activity of the heart. And then, it will be found that many of the children who have been condemned to the abnormal life of the cardiac with all its pitiful demands should, like those unfortunate cases of postural albuminuria, be allowed the lives of normal individuals.

No inference can be made that the author does not agree with the complete protective treatment of organic lesions, but it is his purpose to emphasize the necessity of a full knowledge of the normal—the appreciation of the normal presence of a pulmonary systolic murmur, of an evanescent apical systolic murmur, of sinus arrhythmia and so forth.

There is very little new in the book, but criticism might be extended towards the absence of discussion of certain important cardiac phenomena. There are very few tracings, and their lack is almost always felt when one is dealing with cardiac study. But the author evidently only purposes to pick out interesting features of the cardiac functioning and to expand on them. E. W. B.

Medical Electricity, Roentgen Rays and Radium. By SINCLAIR TOUSEY, M. D. $7.50. (*Philadelphia and London: W. B. Saunders Company, 1915.*)

In this volume of 1200 pages the author has endeavored to cover the field of electrotherapeutics, roentgenology and radium. The portion on electrotherapeutics has been treated pretty thoroughly, and is up to date in literature and therapeutics.

The latter two subjects are still in the developmental stage; and, although the author has taken them up as thoroughly as possible, nevertheless, since the book has gone to press, a great many important discoveries have been made in both these lines. Then, too, on these two subjects the literature has not been kept up to date. The majority of the citations are from monographs published largely between 1906 and 1910, and in only two or three instances are references made to publications as late as 1912. This is especially true in the X-ray diagnosis of gastro-intestinal diseases.

It is unfortunate that the author should have given such a short space to a subject so important that within the last three years it has engaged almost exclusively the attention of the roentgenologists, and in one instance only were we able to find any reference in this particular line of work later than 1912. The subject matter, however, has been handled well, and the salient points are illustrated by numerous cuts.

The mechanics and technique of the X-ray laboratory have been unusually well stated, and in a short space a clear conception is given of that part of roentgenology. The writer has made no attempt to go into details of differential diagnosis. He has simply given a brief description of the lesions and then has relied largely upon his photographic reproductions to illustrate the cases. He has done valuable work in summarizing the results of the various operators as to their findings in various conditions, such as in renal and ureteral calculi, and other kindred subjects.

As a reference work for the literature upon the various subjects, the book is very good indeed, except for the fact that it is not up to date. F. H. B.

A Handbook of Fevers. By J. CAMPBELL MCCLURE, M. D. Cloth, $3.50. (*New York: Paul B. Hoeber, 1914.*)

This compilation on the fevers is written distinctly from the point of view of a decade or two ago, and while pretending "to be no more than a handbook for the use of students and practitioners"

would seem to contain little that would appeal nowadays to the former, and perhaps even to the latter. The clinical descriptions, although poorly balanced, are graphic, and the introduction on the general management of fevers is sound and to the point; but in the sections on therapy the author's practice outweighs at times generally recognized methods of procedure, and in the section on etiology and epidemiology we are constantly surprised by speculation upon questions which for some time have been reduced to facts. Thus it is a shock to hear that "in the dirt and dust of houses, in unclean streets and back courts" the perishable meningococcus "may flourish and spread the disease"; or that diphtheria may arise in connection with some unsanitary spot like an unclean pigsty. Nor do we find any mention of the "carrier" so fundamental in the spread of the latter disease. In the section on therapy we find, in the face of modern views on liberal feeding in typhoid, that a piece of dry bread may be given in uncomplicated cases after the temperature has been normal for seven days. The practitioner is also advised to use opium in typhoid hemorrhage without any warning as to the masking of the early signs of perforation. The discussion of serum-sickness is quite inadequate, since it gives no idea of the actual possible dangers of primary and secondary serum injections. Again, in the employment of immunological terms the author is guilty of a looseness which is certainly unscientific. Thus, for instance, he speaks of plague and meningitis "antitoxins" and of "hypersensitized" instead of sensitized. The bracketing the names of Kolle and Wassermann, with those of Burroughs, Wellcome & Co., as makers of anti-meningitis serum would seem hardly in good taste, and finally, one's sense of the fitness of things is surprised by a section on such a very questionable procedure as the treatment of tuberculosis with contratoxin No. 4, a mixture of coagulant and hemolytic snake-serum and sheep's blood. The inclusion of malaria and kala-azar under the caption of fevers of known bacteriology might be criticised by a purist.

On the whole the book is pleasantly written and quite readable.

A. L. B.

Medical Diagnosis. By Arthur Latham, M. A., M. D., F. R. C. P., and James Torrens, M. B., B. S., M. R. C. P. (*New York: The Macmillan Company, 1915.*)

The authors were of the opinion that there exists a true need for a book in which there is arranged, in a concise and accessible form, all of the clinical information and the more important laboratory details which are necessary for the purpose of making a scientific diagnosis in medical conditions. To supply such a need the present volume of some 600 pages has been prepared, which covers the specific infectious diseases, tropical diseases, diseases of the blood, ductless glands, metabolism, cardio-vascular system, respiratory tract, gastro-intestinal system and the central nervous system. The final section of the book is devoted to certain diseases of the skin.

The method of handling each disease has been worked out along the lines of combining brevity with an excellent oversight of the essential clinical and laboratory findings which make for good diagnoses. It is obvious that not much space can be devoted to any one condition and necessarily some accuracy has been sacrificed to meet the demands of this book. For this reason the reviewer is of the opinion that students would do well to avoid the use of such a volume until after a thorough mastery of the subject had been obtained from larger and more exhaustive textbooks. A number of errors could be pointed out; thus, no mention is made of the phenolphthalein test for kidney function and the urea test given on page 412 has long since been consigned to oblivion by reason of its great inaccuracy. The short section devoted to the examination of the cerebrospinal fluid is practically of no value. The pictures, for the most part, are good, and the 19 colored plates are quite well done. It is certainly unfortunate that none of the ova of the more important worms are pictured.

On the whole the book probably represents as good a compend of medical diagnosis as is at present to be found.

The Salvarsan Treatment of Syphilis in Private Practice. By George Stopford-Taylor, M. D., M. R. C. S., and Robert William Mackenna, M. A., M. D. and B. Ch. Cloth, $1.50. (*New York: The Rebman Company, 1914.*)

This little brochure is written in a pleasant chatty style quite different from the usual treatises. As the authors remark in the preface, the book records rather impressions and conclusions from their own work than a summary of the general status of the subject; hence one inclines less to criticise the frequent trite sayings and truisms scattered through its pages. The exposition of the microscopic methods of spirochetal demonstration is concise and to the point, but the same can hardly be said of the section on serum diagnosis. One is much surprised to find the author still advocating an inaccurate and misleading system which employs the native anti-sheep amboceptor and the complement of the patient's serum. An excellent sketch is presented of the technique to be observed in the preparation and injection of salvarsan and is followed by comments on its general action in the various stages of the disease, illustrated by interesting case reports. The dangers of salvarsan are treated altogether too lightly, but this standpoint is founded on the hitherto fortunate experience of the writers. On the whole, the book, while readable, is not to be recommended to one seeking information, unless he has previously familiarized himself with the subject.

A. L. B.

Public Health Laboratory Work. By Henry R. Kenwood, M. B., F. R. S., Edin. Cloth, $4.00. (*New York: Paul B. Hoeber, 1914.*)

The present volume, of over 400 pages, is divided into six parts, each of which deals with a special subject.

What the author apparently intends to present in this volume is a chemical consideration of the questions arising in relation to public health, since only a brief mention is made of other phases of this type of work. For this reason it fails to meet the full demands of the day. What is needed above all is a compact laboratory manual, which does not narrow its sphere merely to the chemical side of the subject, but in its scope considers, briefly but accurately and comprehensively, the essentials of laboratory diagnosis. In the attainment of this object the science of bacteriology possibly stands first in importance, and yet in this edition hardly any reference to it is to be found.

The subject matter is well presented and the methods outlined, which in many instances do not correspond with the ones adopted by the American Public Health Association, are of considerable merit. They are evidently the summation of years of experience along practical lines. Analytical methods generally are difficult to describe in such a manner as to be both accurate and comprehensive, but in this volume we find them clearly outlined, their relative significance being given in detail without impairment of their comprehensibility.

A brief *résumé* of the subject matter may afford a general conception of the nature and character of the contents. The introductory chapter is of special merit and although somewhat elementary presents the essentials that form the foundation for thorough work along chemical lines. The part dealing with water is especially good. Entirely complete from the chemical standpoint, it also includes a good brief description of the microscopical findings. The standard of pollution—excretal *B. coli* in 10 cc. quantities or less—is worthy of more attention than usually given it. The chapter on air is fairly complete, but a great deal might be added to make it more thorough. The subject matter of the section on milk does not impress one favorably. The

methods of analysis are different from those used in America and in our opinion inferior to them. The discussion of the examination of foods is more satisfactory and considerable attention is paid to lower animal and plant life deleterious to foods. This is a new phase of hygiene which requires more extensive investigation. Such subjects as "Preserved and Tinned Provisions," "Chemical Antiseptics and Tests for These," "Methods of Adulteration" and "Coloring Matters Added to Food" are briefly but capably presented. A discussion on disinfectants concludes the work.

Practical Therapeutics. By DANIEL M. HOYT, M. D. Cloth, $5.00 (*St. Louis: C. V. Mosby Company, 1914.*)

The title is misleading. The book contains no systematic consideration of the treatment of diseases; symptomatic therapeusis is its keynote. "New and Non-Official Remedies" of the Council of Pharmacy of the American Medical Association is included and constitutes the most valuable part of the work.

Practical Therapeutics. By HOBART AMORY HARE, M. D. (*Philadelphia: Lea & Febiger, 1914.*)

That 15 editions of Hare's Practical Therapeutics have appeared in 24 years is sufficient to show that the book is meeting a distinct need in American medicine. It is probably the most comprehensive and most useful one-volume work on practical therapeutics of American authorship.

Child Training as an Exact Science. A Treatise Based upon the Principles of Modern Psychology, Normal and Abnormal. By GEORGE W. JACOBS, M. D. With illustrations. (*New York and London: Funk & Wagnalls Co., 1914.*)

This book, written for the teacher and educator, presents a plea for the training of the individual child according to his needs, rather than for the training of children *en masse*, as now practised in schools. The historical portion of it seems better fitted for the physician and student than for the teacher, who may not be interested in the ups and downs of the education of the feeble-minded with its disappointments and failures up to the time of Séguin. The book is based upon the assumption that every organ of the body has a relation to mental function. The author devotes several chapters to the "Psychology of Childhood," in which he describes first the organs of mental activity—in other words its machinery—and later the steps in the intellectual development of the child. Then follows an account of the psychic abnormalities of the child, whether produced by organic defects, like cretinism, adenoids, imbecility or idiocy, or by functional disorders like hysteria, neurasthenia and the various phobias which weaken the will.

Another section of the book treats of the prophylactic training of the parents, by means of which those suffering from constitutional defects can be prevented by law from marriage or procreation—an impossible task; and of a similar training of children by the use of wise pedagogic methods, nutritious food, gymnastic exercises, manual instruction, kindergarten occupations, Montessori methods and finally sympathetic efforts to form the will and character.

The final section treats of what the author terms the therapeutic treatment of defective children, who, although "burdened," are educable, and also of the uneducable. The book will do good and ought to be read by parents and teachers. It is well illustrated and attractively printed, although disfigured by minor attempts at advanced spelling.

Ionic Medication. By H. LEWIS JONES, M. D. Cloth, $1.50. (*Philadelphia: P. Blakiston's Son & Co., 1914.*)

Dr. Jones attempts to give a "fairly complete record of the actual clinical results which have up to now been gained from ionic medication." The book impresses one as having been compiled by an enthusiast, who is a special pleader. It does not present sufficient proof of the value of ionic medication in any one disease, or in the relief of any one particular symptom, to engender in the reviewer much enthusiasm for the method.

The Principles of Pathologic Histology. By FRANK B. MALLORY, M. D. Cloth, $5.50. (*Philadelphia: W. B. Saunders Company, 1914.*)

The book contains many admirable features. In the arrangement of the subjects discussed the author follows the usual form except as regards the chapter on "Special Injurious Agents and the Lesions they Produce." In this chapter the different disease-producing agents are taken up and the effect of each upon the body and the different organs of the body is discussed in full. The advantage of this feature is quite distinct. Another important change is the introduction of a new classification of tumors, which renders the subject much more clear and comprehensible. The inclusion of the leukæmias and of Hodgkin's disease under this head, however, is open to discussion, more especially in the light of our present knowledge of the latter disease.

Throughout the book, the text is clear and concise. The introduction of the term "endothelial leucocyte," applied to a type of cell, and its application throughout the book to a class of cells are apt to lead to some confusion. In many instances where there are divergent views on certain points, Dr. Mallory has given the one that he considers to be correct, but neglects to mention the opposing views. This, and the fact that practically no references are given to the literature on the subjects discussed, make the book rather a monograph than a text-book.

The illustrations are wonderful and add greatly to the attractiveness of the volume. As a whole, Dr. Mallory's book is a great addition to the literature on pathology.

BOOKS RECEIVED.

Obstetrical Nursing. By Charles Sumner Bacon, Ph. B., M. D. Illustrated with 123 engravings. 1915. 12°. 355 pages. Lea & Febiger, Philadelphia and New York.

Diseases of the Bronchi, Lungs and Pleura. By Frederick T. Lord, M. D. Illustrated with 93 engravings and 3 colored plates. 1915. 8°. 605 pages. Lea & Febiger, Philadelphia and New York.

Infant-Feeding. Its Principles and Practice. By F. L. Wachenheim, M. D., 1915. 12°. 340 pages. Lea & Febiger, Philadelphia and New York.

Student's Manual of Gynecology. By John Osborn Polak, M. Sc., M. D., F. A. C. S. Illustrated with 100 engravings and 9 colored plates. 1915. 12°. 414 pages. Lea & Febiger, Philadelphia and New York.

Quain's Elements of Anatomy. Eleventh edition. Editors, Sir Edward Albert Schafer, LL. D., Sc. D., M. D., F. R. S., Johnson Symington, M. D., F. R. S., and Thomas Hastie Bryce, M. A., M. D. In four volumes. *Vol. IV. Part I. Osteology and Arthrology.* By T. H. Bryce. With 247 text figures and 28 colored plates. 1915. 8°. 329 pages. Longmans, Green & Co., London, New York, Bombay, Calcutta and Madras.

The Alimentary Tract. A Radiographic Study. By Alfred E. Barclay, M. A., M. D., B. C. (Cantab.), M. R. C. S., L. R. C. P. 1915. 8°. 195 pages. The Macmillan Company, New York.

United States Army. Index-Catalogue of the Library of the Surgeon General's Office, United States Army. Authors and Subjects. Second Series. Vol. XIX. U.—UZIELLI. 1914. 4°. 674 pages. Government Printing Office, Washington.

Nursing and Care of the Nervous and the Insane. By Charles K. Mills, M. D. Third edition. Revised by the author, assisted by N. S. Yawger, M. D. 1915. 12°. 142 pages. J. B. Lippincott Company, Philadelphia and London.

The Commoner Diseases. Their Causes and Effects. By Dr. Leonhard Jores. Authorized English translation by William H. Woglom, M. D. With 250 figures in the text. 1915. 8°. 424 pages. J. B. Lippincott Company, Philadelphia and London.

Differential Diagnosis. Volume II. Presented through an analysis of 317 cases. By Richard C. Cabot, M. D. Profusely illustrated. 1915. 8°. 709 pages. W. B. Saunders Company, Philadelphia and London.

Dissection Methods and Guides. By David Gregg Metheny, M. D., L. R. C. P., L. R. C. S. (Edin.), L. F. P. S. (Glas.). Illustrated. 1914. 8°. 131 pages. W. B. Saunders Company, Philadelphia and London.

A Laboratory Manual and Text-Book of Embryology. By Charles William Prentiss, A. M., Ph. D. With 368 illustrations, many of them in colors. 1915. 4°. 400 pages. W. B. Saunders Company, Philadelphia and London.

A Practical Text-Book of Infection, Immunity and Specific Therapy. With Special Reference to Immunologic Technic. By John A. Kolmer, M. D. With an introduction by Allen J. Smith, M. D., Sc. D., LL. D. With 143 original illustrations, 43 in colors. By Erwin F. Faber. 1915. 8°. 899 pages. W. B. Saunders Company, Philadelphia and London.

A Text-Book of Diseases of the Nose and Throat. By D. Braden Kyle, A. M., M. D. With 272 illustrations, 27 of them in colors. Fifth edition, thoroughly revised and enlarged. 1914. 8°. 856 pages. W. B. Saunders Company, Philadelphia and London.

Diagnostic and Therapeutic Technic. A Manual of Practical Procedures Employed in Diagnosis and Treatment. By Albert S. Morrow, A. B., M. D. With 860 illustrations, mostly original. Second edition, thoroughly revised. 1915. 8°. 834 pages. W. B. Saunders Company, Philadelphia and London.

Cancer: Its Cause and Treatment. By L. Duncan Bulkley, A. M., M. D. 1915. 12°. 230 pages. Paul B. Hoeber, New York.

Nature and Nurture in Mental Development. By F. W. Mott, M. D., F. R. S., F. R. C. P. With diagrams. 1915. 12°. 151 pages. Paul B. Hoeber, New York.

The Difficulties and Emergencies of Obstetric Practice. By Comyns Berkeley, M. A., M. D., M. C., Cantab., F. R. C. P., Lond., M. R. C. S. Eng., and Victor Bonney, M. S., M. D., B. Sc. Lond., F. R. C. S. Eng., M. R. C. P. Lond. Second edition. With 302 illustrations. 1915. 8°. 807 pages. P. Blakiston's Son & Co., Philadelphia.

Diseases of the Skin. By James H. Sequeira, M. D. Lond., F. R. C. P. Lond., F. R. C. S. Eng. Second edition. With 48 plates in color and 238 text figures. 1915. 8°. 650 pages. P. Blakiston's Son & Co., Philadelphia.

Diabetes Mellitus. By Nellis B. Foster, M. D. [1915.] 8°. 243 pages. J. B. Lippincott Company, Philadelphia and London.

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